BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 31.] 1934. [No. 9.

THE PREVENTION OF ASCARIS INFECTION: A CRITICAL REVIEW.

By Lieut.-Colonel Clayton LANE, M.D., I.M.S. (retd.).

Sectional Editor, Tropical Diseases Bulletin.

(Received June 28, 1934.)

The literature studied below deals with the conditions in which the infective larva develops within the ascaris egg after it leaves the human body, with its mode of re-entry into this, and briefly with its migrations within the body as it passes to its adult habitat in the small intestine. In considering the measures which should be taken to prevent infection, it is pointed out that too little weight seems to have been given to the pig, or to air convection.

THE BIOLOGY OF THE EGG.

Of course it is only the fertile egg which can develop. The unfertile egg, recognized as such over 30 years ago, has been studied and pictured in its various forms by OTTO (1932, **29**, 751)* and KELLER (1933, **30**, 684). The former basing his remarks on the examination of over 50,000 eggs found 15·9 per cent. of them to be unfertile, emphasized the ease with which the outer albuminous coat is dissolved in decinormal caustic soda solution, and noted the occasional presence of a triangular unfertile form; he added that the solitary female worm might produce either fertile or unfertile eggs. †Keller reported that unfertile eggs were commonest in infections with 1 to 5 females;

* References, unless otherwise stated, are to summaries in this *Bulletin*, the first figure giving the year, the second, in blackface type, the volume number, and the third the page of the *Bulletin* containing the summary in question. Where the year of publication of the original paper differs from the year of publication of the *Bulletin* summary, two dates are given—the first in brackets referring to the original paper, and the second to the *Bulletin* summary.

† ESSED & VAN THIEL (*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Apr. 24. Vol. 74. No. 9. pp. 551–552. With 4 figs. on 1 plate) report a case in which polar thinning of the shell in some unfertile eggs gave the appearance of an operculum.

when there were more than 5 of these the percentage of unfertilized eggs decreased. YOKOGAWA and WAKEJIMA (1932, **29,** 737) reported, however, that unfertile eggs were commoner in heavy than in light infections. YOSHIDA and TAKANO ((1923) 1924, **21,** 218) showed that fertile eggs readily lost their outer shell in artificial gastric juice, so that a person passing decorticated eggs in the faeces may merely have swallowed them. No such coprophagic suggestion is of course tenable if the faeces are being examined in caustic soda solution, which also decorticates them.

Physical Factors Influencing Survival and Development of the Egg.

Temperature.—BAKKER (1924, **21,** 959) showed that temperatures of −30°C. to −190°C. were deadly to the eggs, while one of −15°C. had no influence on further development at 25°C.; temperatures between −15°C. and −30°C. killed some eggs and delayed subsequent development of the survivors, the proportion of those killed and damaged increasing in proportion as the temperature fell and the duration of exposure lengthened. CRAM (1924, **21,** 958) showed that eggs become less resistant to cold as their development progresses, an observation confirmed by PANAGIA (1933, **30,** 684). Thus, when freshly passed, an exposure of 40 days to temperatures of −2°F. to −16°F. (−19°C. to −27°C.) did not prevent development when the temperature became favourable; when partly developed the eggs similarly withstood such a temperature for 20 days; and although the lifespan of the developed embryos was thereby shortened they nevertheless remained infective to guineapigs. MARTIN ((1926) 1928, **25,** 960) found that at temperatures from −5°C. to +10°C. eggs could survive for 2 years in a dry medium and for four years in a moist one. These exactly measured experiments amply confirm those of YOSHIDA ((1920) 1921, **17,** 80) that eggs in or on the ground survive the winter in Osaka, Japan, and of MARTIN that they resist freezing and are viable after lying in the soil of Nebraska all winter. BROWN (1928, **25,** 958) confirmed the results of other workers that the eggs are completely embryonated in 23 to 26 days at 21°C. and in 10 to 11 days at 30°C.; and noted that on raising the temperature from the one point to the other each stage of development was equally quickened—2½ times. At body temperature development stops when 4 to 8 cells have been formed, at 70°C. all are killed (WHARTON, 1915, **6,** 304). OGATA ((1924) 1925, **22,** 882) reported that at 70°C. only one second is needed to effect this, but at 65°C. sixty seconds.

Oxygen.—BROWN (*l. c.*) showed that each egg consumed about 0·0000026 cc. of oxygen during its development whatever the temperature, that with an oxygen tension of 2·1 to 2·6 cc. per litre of water (or about half the normal) development proceeds normally, but that when it is as low as 1·1 cc. per litre this is slowed. It is not lack of oxygen which stays development at 37°C., for at that temperature its volume is 4·5 cc. per litre. Further Brown showed that embryonated eggs were not injured by a stay in oxygen-free water of 6 weeks or more, so that such eggs would survive at least for a time at the bottom of a pond where the water did not contain enough oxygen for development.

Moisture.—It seems impossible to measure with accuracy the amount of water in the surroundings of eggs by means which will not dehydrate the egg itself, but it appears that all surrounding water can be lost without injuring the egg. WHARTON (*l. c.*) noted that while drying did not kill the egg a small amount of water was necessary for development.

RANSOM and FOSTER ((1917) 1918, **12,** 186) reported that drying delayed development, but that this was resumed on wetting. That dried eggs can survive for as long as 2 years at temperatures as low as −5°C. has been noted. MANALANG (1927, **24,** 997) placed in a desiccator for 7 days eggs which had been dried on to a slide; when placed in Kroneker's fluid larvae developed, and some maintained mobility for a further 27 days. BROWN ((1928) 1929, **26,** 548) found that when embryonated eggs were allowed to dry on glass all were dead in 37 days, nearly all in 28 days, and many after 7 days. The dried but living eggs developed a bubble within them which was pushed about by the moving embryo. SPINDLER ((1929) 1930, **27,** 972) reported from South-West Virginia that viable embryonated ascaris eggs were always found in unshaded dry dooryards of familes whose members were infected with the parasite.

Sunlight.—The last observation raises the question of the effects of light apart from heat. In BROWN's experiments no difference was found between cultures exposed to and shaded from the sun, the maximum temperature being 90°F. (32·2°C.) except on one day when it reached 101°F. (39°C.). MANALANG (1927, **24,** 997) found that eggs failed to develop when dried on a slide and exposed to sunlight for 1½ hours; if suspended in Kroneker's fluid light was lethal in 2 hours.

Chemicals.—The extraordinary impermeability of the ascaris shell is well known. YOSHIDA ((1918) 1921, **17,** 79) summed up the matter thus. Embryos develop within the eggs in the following percentages of chemicals; hydrochloric acid 0·7, carbolic acid or nitric acid 0·3, acetic acid 4, formalin 5 [dilute formalin is a favourite culture medium], corrosive sublimate 0·7, common salt 7·5, sodium hydrate 1·0. He reported urine to be soon fatal to them; but MANALANG found motile embryos in eggs after nine days culture with it, this being a normal interval in the conditions of his laboratory. These strengths it will be noted are not those which cannot be exceeded without harming the egg. As to acidity SCHMELEWA ((1929) 1931, **28,** 226) experienced no retardation of development when pH remained between 3 and 8.

Hatching.—There has long been uncertainty as to the conditions which induce hatching. Thus YOKOGAWA ((1923) 1924, **21,** 215) could merely put them generally as—full development of the embryo with suitable temperature, and possibly embryonic activity stimulated by intestinal peristalsis. It can hardly be a mere question of action of the digestive juices of the host, for MANALANG (1927, **24,** 997) had no hatching when eggs 4 months old with motile embryos were kept in duodenal or ileal contents obtained from man within an hour of death, or in 0·2 per cent. hydrochloric acid or sodium hydroxide, although the embryos remained motile for 2 to 4 weeks. KONDO ((1920) 1922, **19,** 233) reported that ascaris eggs cultured out of doors in animal charcoal which was kept moist and away from direct sunlight reached maturity in 70 days, and a few days later hatching began, the larvae being then capable of living in wet soil for more than a month. The only condition which seems to have been reported as inevitably producing rupture of the eggshell is drying followed by moistening (BROWN, 1928, **26,** 548); he noted (*v. supra*) that with drying a large bubble forms, presumably of gas, which the active embryo pushes about as it moves; on moistening, water seemingly re-enters the shell and causes increased tension since the contents are prevented from swelling to their natural size by the imprisoned bubble, and the shell bursts. Whether KONDO's act of keeping cultures moist really meant wetting when the culture dries does

not appear from the English summary. DANHEIM (1925, **22,** 879) had previously reported that moistening of dried eggs of *Ascaris equi* caused them to hatch.

Longevity of the egg.—Among modern reported instances is that already noted of MARTIN—2 years when dry and 4 years when humid.

THE FECUNDITY OF ASCARIS AND ITS IMPLICATION.

By dissecting out the genital systems of two adult female worms, imbedding in celloidin portions from different levels, sectioning these, and counting the number of eggs in several sections from each level, CRAM (1925, **22,** 883) estimated the number of eggs developed or in process of development at any moment as being from 26 to 27 millions; considerably less than the computations of ESCHRICHT or LEUCKART. BROWN and CORT ((1927) 1928, **25,** 464) comparing egg counts with worm recoveries in 2 cases put the eggs produced daily by each female worm as nearly a quarter of a million, MORETTI ((1928) 1930, **27,** 974) as 107,000 in one child, and MANALANG (1928, **25,** 960) as 1,420 to the gram [or 284,000 daily if the count was on the mushy 200-gm. stool common in the tropics]. On the other hand the numbers of adult worms harboured by any person are mostly quite few. TWINING ((1930) 1931, **28,** 688) published 475 as a supposed record, and although this is very far from being so, such a number as this is very rarely even approached. The chances must be millions to one against any particular egg resulting in an adult worm. The conditions, then, which have to be fulfilled before adult life can be attained must be reached with great rarity.

THE RELATIONSHIP OF ASCARIS IN MEN AND SWINE.

The old conviction that worms from the two hosts are morphologically indistinguishable is, with one questionable exception, fully confirmed (*e.g.*, RANSOM and FOSTER 1919, **14,** 153; SCHWARTZ 1920, **16,** 146; KOIDZUMI *et al.* (1925) 1927, **24,** 187; THORNTON 1924, **21,** 573). BARKER (PAYNE *et al*, 1925, **22,** 488) found the number of chromosomes in the two forms to be 48, though KOIDZUMI *et al.* stated that the haploid number in the human form appeared to be 12 and in the porcine 13. But it is held that there are nevertheless biological differences which those of that turn of mind hold sufficient to justify the use of two specific names; *Ascaris lumbricoides* for the parasite of man, and *A. suum, A. suis,* or *A. suilla* for that of the pig. Facts on which this conclusion rests need detailed consideration, for the matter is one of great hygienic importance.

STEWART (*Parasitology*, 1917, vol. 9, p. 213) used two pigs two months old. One was fed on 13 occasions with many thousands of ripe eggs 26 to 64 days old from the pig; when killed at five months a single small ascaris was found in the intestine. The other was on 9 occasions fed with large quantities of ripe eggs 22 to 106 days old from man, but no eggs appeared in the faeces; so when it was still under 4 months old and till it was 5 months old it had given to it large quantities of eggs from the pig 17 to 73 days old, but no eggs appeared in its faeces after an interval sufficient for their growth to the adult stage. There is no evidence here of two strains. Similar is the conclusion which follows from experiments in which STEWART ((1917) 1918, **11,** 81; 1918, **12,** 187) fed pig ascaris eggs to six pigs in such numbers that 1,000 larvae must, it was believed, have reached the trachea in each case. "Two of the pigs suffered from acute pulmonary ascariasis, a third from a slight attack

. . In five cases no intestinal worms resulted, in one case intestinal worms may have resulted but they may also have been due to accidental infection." Here ripe ascaris eggs from the pig signally failed to infect pigs. RANSOM and FOSTER too ((1917) 1918, **12,** 186) failed to infect pigs, and in most of their experiments eggs from the pig ascaris were used. STEWART again (1919, **13,** 212 ; (1919) 1920, **15,** 230) fed ripe eggs of the pig ascaris to pigs which were 4, 4 and 70 days old. The first was fed with 22,000 eggs, and large numbers of young worms 3·8 mm. long were found when it was killed on the fourteenth day ; the second was also fed with 22,000 eggs and showed an ascaris pneumonia, but not a single worm was found when it was killed on the nineteenth day ; the third was fed with 50,000 eggs but showed no worms when the gut was opened on the thirty-first day. SCHWARTZ (1920, **16,** 146) found a biological identity between the two forms so far as immunological tests showed. STEWART ((1920) 1921, **18,** 122) fed four sucking pigs with ripe eggs of ascaris from the pig, one died of ascaris pneumonia, the other three showed small worms in the intestine when examined on the fifteenth. seventeenth and nineteenth days. Further he reported (1920, *Trans. Roy. Soc. Trop. Med. & Hyg.*, vol. 14, p. 20) feeding two pigs with ripe eggs of the pig ascaris, on the fourteenth day both had severe pneumonia, on the nineteenth day one had numerous small worms in the intestine, the other had none. KOINO ((1922) 1923, **20,** 235) gave 500 ripe ascaris eggs from the pig to a volunteer and took 2,000 from man himself. Both suffered from rigors with fever and marked pulmonary symptoms ; after an anthelmintic 50 days later the volunteer passed no worms and Koino passed 667. He adds " The conclusion is that while ascarids from the pig and man are morphologically similar there is a biological strain of pig ascaris capable of causing pneumonia in man, but incapable of reaching the adult stage in this host." It is merely necessary to refer back to the last of STEWART's quoted experiments to be satisfied that no such conclusion emerges from the facts of these two feedings. PAYNE, ACKERT and HARTMANN (1925, **22,** 488) fed several thousand eggs of the ascaris of man to five pigs, all showed " thumps " (that is hurried breathing), but in none did intestinal infection occur ; no parallel infection of pigs with pig ascaris was attempted as a control. Again, one of these writers swallowed 54 mature pig ascaris eggs without becoming infected ; another who had formerly become infected with ascarids after five years engaged in the directing of hookworm campaigns (for which reason that infection was judged to have been of human and not of porcine origin) swallowed embryonated eggs of the pig ascaris and suffered no infection. Lastly MORGAN ((1931) 1932, **29,** 59) fed three pigs when 2 months and again when 3 months old with large numbers of embryonated eggs of the pig ascaris ; they had no symptoms and passed no eggs.

The importance of this summary is that it is believed to comprise the whole of the evidence published since this *Bulletin* came into existence, on which it is assumed that the ascaris of man and pig, though anatomically indistinguishable, are physiologically distinct. It is singularly unsatisfying, being based on a few instances in which feeding from man to pig or pig to man have failed to infect, whilst ignoring the more numerous and striking ones in which eggs of ascaris from the pig have failed to infect pig. It is clear that in this matter controls have been quite inadequate. FÜLLEBORN's reading of the evidence ((1931) 1932, **29,** 751) was that swine eggs infect man but eggs

of human origin do not infect swine. At all events the reviewer can see no justification for neglecting the pig as a source, and perhaps a potent source, of human infection.

Obviously there are quite unknown factors at work in preventing maturation of pig ascaris eggs in pig; one of them, as has been pointed out in Japan, lies in the effects of vitamins. KOIDZUMI, HIRAISHI & KOINO ((1925) 1927, **24,** 187; 1927, **24,** 997) reported that pigs fed on eggs whether of porcine or human ascaris failed to mature, but when vitamin A was withheld from their diet they easily became infected with either type of egg, though the infection with eggs from man was never so plentiful as with those from the pig. These results appear to have been fully confirmed by HIRAISHI ((1926) 1927, **24,** 998). Correlation of infections in man and pig have been made by COPEMAN (1925, **22,** 881) and STIVEN (1925, **22,** 883). Another possible factor is considered below, namely the suggestion that the alimentary canal is not the optimum portal of the entry of this infection.

MODES OF INFECTION.

BROWN (1927, **24,** 998) refers to three modes of infection: (*a*) Embryonated eggs may be eaten stuck to vegetables or otherwise taken in with food, under which heading he adds these words. "In the homes surveyed [in Panama] it was customary for the children and sometimes the adults to sit or squat on the floor while eating from a dish which was placed on the floor or on a small bench. This combination of living so close to the floor of their abode with the promiscuous defecation upon it by the children would naturally be suspected as a source of infection by ascaris." (*b*) They may be taken in drinking water. (*c*) He adds "Even windblown dust has been suggested as a source of ascaris infection." To this list must be added the possibility of infection by the skin.

1. *Infection by Mouth.*

i. *The route taken by larvae when eggs are swallowed.*—That infection may be produced by swallowing eggs has been known since GRASSI's time and has been instanced above, and it was then assumed that the embryos were hatched in the alimentary canal and there grew into adults. STEWART's experiments on rats and mice (1916, **8,** 197) were the first to suggest that things were otherwise, for when he fed them on embryonated eggs the larvae were found in the lungs of these animals. Stewart was of opinion that they acted as intermediate hosts, passing on infection by being eaten by pigs, or by nibbling man's food and moistening it with their saliva, in which fluid he had found larvae. It was immediately pointed out in the *British Medical Journal,* and shortly afterwards over their signatures by others, that the then known facts were more reasonably explicable by assuming that the larvae hatched in the alimentary canal, bored by virtue of a thigmotaxy into its wall, reached the lung by the blood vascular escalator, were carried by the bronchial cilia to the larynx, and were swallowed—that there was here another instance of a route of infection established as occurring in the life histories of hookworms and strongyloides. That in the optimum host the larvae reach the lung by boring out of the alimentary canal is not now questioned; YOSHIDA, however ((1918) 1920, **15,** 230, etc.) maintained that in such a host larvae bore through its wall into the peritoneal cavity and thence through the diaphragm and pleurae into the lungs; though he found in fact no larvae in the pleural cavity

and many in liver and lungs. The point was investigated numerically by RANSOM and CRAM ((1921) 1922, **19,** 234). After an infective feed larvae became very numerous in the portal vein, liver, vena cava and right heart in 17 to 24 hours, numerous in the mesenteric glands in 20 to 24 hours, though after 5 days these contained as many dead as living larvae. In the abdominal cavity none appeared for 3 days, and after that they were found in small numbers only, and in a fraction only of the infected. In the pleura the greatest numbers were found in 6 to 7 days and they had developed considerably. A few scattered larvae were found in peripheral lymph nodes within 24 hours of infection and in the thyroid and thymus; FÜLLEBORN ((1921) 1922, **19,** 234) found them in the kidney after this organ, except for the hilum, had been enclosed in a rubber sheet through which larvae cannot bore, and in the brain, as well as, so far as belascaris goes, in the foetus ; ISHII and YAMASHIRO (1932, **29,** 752) found them invariably in the urine of rabbits which had been fed with 200,000 mature eggs, OHBA (1925, **22,** 882) invariably as well as red corpuscles in that of heavily infected animals, SUYEMORI (1925, **22,** 487) in the eye, OTAKE ((1928) 1929, **26,** 551) in the mammary gland. These observations form evidence, which most will consider conclusive, that the lymph escalator from the alimentary canal is not a favourable one, but that the use of the blood escalator would give such a distribution as has actually been observed. The use of the pulmonary escalator was proved directly for man by KOINO ((1922) 1923, **20,** 235), who found larvae in the sputum from the ninth to the sixteenth day after a deliberate infection, 178 being so detected on the 11th day alone ; for fortuitous infection the same has been reported by LEITCH ((1929) 1930, **27,** 974) on 4 occasions during the invasion stage, and by BIRK (1933, **30,** 684).

ii. *Eating embryonated eggs.*—That this may on occasions result in experimental infection has been amply shown above. As to its producing natural infection, PANTIN ((1918) 1919, **13,** 212) noted that bitter experience convinced her that vegetables fertilized with nightsoil were a most sure cause of infection, and COPEMAN (1925, **22,** 881) attributed a local endemic in Hertfordshire to this cause. ISOBE ((1925) 1926, **23,** 257) reported from Formosa 13 ascaris eggs on a single spinach plant, 2 embryonated eggs on an onion and one on a cabbage ; WALKER (1927, **24,** 998) considered eggs on vegetables as being responsible for an ascaris incidence of 87·71 per cent. in one battalion at Singapore. ISHIKAWA ((1929) 1931, **28,** 225) showed that vegetables manured with the " bricks " into which heaped manure is fashioned in Manchuria carried ascaris eggs ; while the inner parts of such " bricks " retain moisture, and from them were obtained viable eggs even after exposure to summer heat and severe winter cold. Similarly, to vegetables manured with human faeces was attributed infection in Tura Prison, Egypt (KHALIL, 1931, **28,** 665), ova being found in the soil adherent to them in the jail kitchen. STEKHOVEN (1931, **28,** 666) had a like experience in the island of Terschelling ; YOSESATO and SUMI (1932, **29,** 739) put the percentages of vegetables bought in Mukden and bearing worm eggs, largely those of ascaris, as : lettuce 92, spinach 54, radish 43, onion 33, cabbage 17, potato 8. As to the second means considered under this heading by BROWN, his meaning seemingly is that food is infected by hands which have been touching or resting on a floor contaminated with embryonated ascaris eggs, or that such fouled hands are themselves licked or sucked. There is, however, always the chance of infective dust being blown on to food, or being left on it by flies.

iii. *Drinking embryonated eggs.*—The likelihood of this method of natural infection was reaffirmed by CHANDLER ((1925) 1926, **23,** 265 ; (1926) 1927, **24,** 190, 191) thus: " The fact that the defaecation areas are commonly situated on the banks of hulas [ponds], and that in the dry season the hulas themselves are used as defaecation sites, suggested that the water in the hulas might be responsible for the abundant and heavy infections with these parasites." And again " It is very obvious that on this island the tanks must be nearly all grossly polluted." On the other hand, certain villages " gave remarkably low incidences of ascaris and trichuris infections considering the fact that the tanks which they used for drinking were grossly polluted." Embryonated ova were not sought for in any case ; while in the earlier ones the argument seems to depend much on what the writer would expect to occur, and in the last instance the facts were clean against the presuppositions.

2. *Infection through the Skin.*

K. KONDO ((1920) 1922, **19,** 233) smeared hatched larvae on the skin of guineapigs and recovered them from the lungs later, observations confirmed by ASADA ((1921) 1922, **19,** 657) and stressed by MAPLESTONE ((1928) 1929, **26,** 548). It is not stated in the English abstracts of the Japanese papers what steps were taken to insure that the guineapigs did not lick the spots on which the larvae had been placed, and the reviewer has hitherto been unable to obtain further information. Previous to this, RANSOM and FOSTER (1919, **14,** 153) had injected embryonated eggs under the skin of guineapigs and had recovered larvae from the lungs. What, if any, effect a perspiring skin may have in freeing an embryo from a dried egg which has landed on it, so paving the way for cutaneous infection, is quite unknown.

3. *Breathing in of Embryonated Eggs.*

Infection by air conveyance to food has just been mentioned, flies being possible conveyors of eggs by this medium. That a privy might have a radius of action infective for neighbours was shown by STILES ((1915) 1916, **8,** 209) for ascaris among other infections, and entry of infection into the new host was held to be coprophagic, faecal matter being conveyed to food probably by flies and so eaten. But what is here in mind is infection by inspiration—the breathing in of embryonated eggs as dust—the evidence for which, in spite of the " even " in the quotation from BROWN (above p. 610) seems to the reviewer to have steadily increased since he first formally suggested it (Discussion : STEWART 1920, *Trans. R. Soc. Trop. Med. & Hyg.*, Vol. 14, p. 20) ; but it is circumstantial and inferential, no direct experiments having ever been reported. It is clear that such a mode of infection spares larvae a transit through the liver which is presumably a handicap to them, and such transit, it is suggested, should be considered as a possible reason for the repeated failures to infect pigs with ripe ascaris eggs from the pig, that mode of infection not being the optimum one.

Three considerable investigations bearing on this matter have been published during the last eight years—from China, the Southern United States, and Panama ; in each case the pertinent material is contained in more than one paper, so that these have to be compared to get a proper view in attempting evaluation. The points apposite to the present review are these.

CORT and STOLL ((1931) 1932, **29,** 416) reported the degree of ascaris incidence among nearly 4,000 persons living in 5 different areas in China.

In all areas human faeces are used as fertilizer ; in two they are stored dry and in three wet. In making dry fertilizer (CORT *et al.* (1926) 1927, **24,** 193) faeces are mixed with clay and straw, and the mixture piled outside towns or along village streets and there left to dry ; in making wet fertilizer faeces are kept in liquid form in vessels until the time comes to spread them on the fields. In the two districts in which dry fertilizer is used the respective incidences of ascaris infection were 90 and 86 in males and 94 in each in females. One lay in the dry region of North China and in it footbinding was almost universal, so prohibiting women's work in the fields ; while in the other the climate was considerably milder with heavier rainfall, and there was little footbinding. In the three districts using wet fertilizer the percentage incidence in males was 58, 45 and 63·5, the corresponding figures in females being 70, 75 and 77, the women being field workers and footbinding little or rare. The five districts thus fall into two intensity groups, and the only reported factor which is common to all members of each group is the kind of fertilizer prepared by its members ; and clearly the mode of manufacture used in the dry method must favour distribution of ascaris ova as dust. A confirmatory experience is that of KHALIL ((1933) 1934, **31,** 327) in the Siwa Oasis of Egypt, in which ascaris infection is very heavy and dried human faeces are collected from house latrines and used as manure.

In the Southern United States the outstanding attitude of those who have recently investigated ascaris infection there is concisely summed up in OTTO's words (1932, **29,** 749) : " The sanitary privy [a pit privy] or in fact most any type of privy no matter how obnoxious if used by all members of a family will effectively control infestations with these parasites." Again OTTO and SPINDLER write ((1930) 1931, **28,** 174), " The introduction of the privy, however, has apparently done little to control the Ascaris burden in many areas because regardless of the presence or absence of a privy the younger children deposit their stools close to the house and in playgrounds where eggs are readily conveyed by dirty hands and food to the mouth."

These are not, however, conclusions proceeding from observations. They are conjectures. But the matter has in fact been tested in Panama in conditions which at least approach to those of control of single factors, and the conclusions which emerge from these seem to the reviewer to be quite different. Here there lie two adjacent villages, Marica Arriba and Sardina (CORT *et al.* (1929) 1930, **27,** 421), each on the same subsoil, each strung along a horse trail, with similar houses set in small cleared areas, and with cultivation or rank jungle coming to within five or ten yards of them ; further, each village contained 121 inhabitants. " Sanitary " latrines, which were in fact pit latrines (CORT *et al.* (1929) 1930, **27,** 431), were built in Sardina in November–December, 1925, and surveys made thereafter showed that a very great reduction in soil pollution occurred ; the privies were being largely used. Marica Arriba was left " unsanitated " and, as just stated, conditions as between the two villages closely approached to the control of that single factor. At the first stool examination, made in July, 1926, that is to say after privies had been in use in Sardina for 8 or 9 months, " sanitated " Sardina had an average egg count per cc. of 23,190 and Marica Arriba one of 16,100 ; at the last examination made in February, 1927, the average count in " sanitated " Sardina had risen to 48,540, and in unsanitated Marica Arriba had fallen to 13,010. The outstanding fact is that in spite of a great reduction of soil pollution in Sardina ascaris

infection markedly increased. Here again it was to children that such soil pollution as persisted was attributed in Sardina ; but in Marica Arriba, where things were as they had been, children of course continued to pollute it. To attribute the increased infection in Sardina to soil pollution by children implies that to stop the fouling of soil by adults will increase in some way the infectivity of eggs contained in the faeces of children if these only are deposited on the soil. That view will hardly appeal to medical sanitarians. The position is that the building and use of " sanitary " privies was followed by, and that it presumably caused, a marked increase in ascaris infection, for these constituted the only discoverable and reported differences between these two neighbouring villages. It does not seem that the increase in infection in Sardina is explicable on grounds other than its air convection, for most of its inhabitants were now religiously visiting the latrines—spots where faeces were accumulated—and the density of eggs if air-borne must be greatest just in those places, diminishing apparently as something like half the cube root of the distance from their source This line of argument assumes that skin infection by hatched larvae need not be reckoned with ; but in either case it was the privy which spread the infection.

The reviewer's own experience is apposite here. During his Darjeeling inquiry which covered faecal examinations on 30,000 persons (LANE, 1916, *Indian Jl. Med. Res.*, Vol. 4, p. 274 ; 1917, *ibid.*, Vol. 5, p. 350) he found that on only two of ten tea gardens were the coolies provided with latrines, and that these had been in use for a number of years. In one garden the latrines were of the drop privy type—platforms built out from the steep hillside—faeces dropping through holes in them to land and remain stinking further down the slope. On that garden ascaris infection was greater than on any other, namely 82·88 per cent. against an average of 69·4 for the other nine. Manifestly the conditions in the garden with drop privies were almost ideal for aerial convection and ill-fitted for any other kind.

Another pertinent investigation in Panama is that by BROWN (1927, **24,** 998) at Penemone, two miles from the villages dealt with in the last paragraph but one. From 201 gm. of sweepings collected from the interior of seven huts he isolated 29 developing, 8 viable embryonated, and 9 degenerated eggs, or 46 in all ; from 20 gm. of soil from the yard of a hut the corresponding figures were 11, 3 and 3, or 17 in all ; and from 20 gm. of soil taken from under the eaves of a hut he isolated 24,000 eggs, all being in developing stages or degenerated. As noted, he seems to ascribe the heavy infections which actually occurred in these households to an acquisition during feeding within the houses. In point of fact eggs were far more numerous outside than inside the dwellings, and their distribution seems to correspond with that which would occur were developing eggs blown into dwellings by draughts. CORT ((1931) 1932, **29,** 59) points out rightly that the presence of ascaris can be used as an index of the local status of sanitation ; accepting this standard, it is noteworthy that the incidence of ascaris infection has been increased in different parts of the world by the building of privies, even those that are labelled " sanitary." As the writer has suggested ((1932) 1933, **30,** 55) to provide a village with latrines and label it " sanitated " is to confuse faith and works. Experiments to test the possibility or ease of infection by the inbreathing of ripe eggs seems never to have been undertaken.

Prevention.

The prevention of ascaris infection does not, then, lie in the installation and use of pit privies. Whether the anaerobic state and fermentative conditions in the septic tank privy will do so, must seemingly depend on whether decomposition in the fluid medium can be depended on to destroy these eggs in all conditions within a given time. Stiles (1911, Publication No. 2, Rockefeller Sanitary Commission) reported that, after four months in the miniature L.R.S. septic tank privy, about a fifth of the ascaris eggs appeared to be alive. The Beccari process (*Bulletin of Hygiene*, 1931, Vol. 6, p. 191) of refuse disposal will raise the temperature of the vat to 70°C., and if it does so throughout will be successful in killing all ascaris eggs. It has been used with encouraging results on a relatively small scale for stable manure (Schwartz *et al.* 1931, U.S. Dept. Agric., Yearbook of Agriculture, p. 353). Low temperatures ordinarily met with seem to have no practical hygienic importance. The adequate scalding of vegetables which will be eaten raw kills eggs adhering to them. Disinfection of faeces by chemicals is an unpromising line of attack and the action of urine remains in doubt, as does that of sunlight. Drying kills eggs in due time; yet drying means dust. But to dry and then moisten viable eggs is the only way hitherto reported in which hatching of the embryo can inevitably be brought about, and it is noteworthy that such conditions will be very exactly reproduced when viable eggs inbreathed as dust come to rest on the mucosa of the air passages. The experimental evidence which claims to show the lack of infectivity for man of ripe ascaris eggs from the pig is quite unconvincing (there is perhaps epidemiological evidence in the opposite direction) and to disregard the pig as a potential source of ascaris infection in man seems to the reviewer to be wholly unjustifiable.

The risk of air convection has hitherto been almost wholly disregarded, though it seems the best explanation of a good deal in the present anomalous and confusing position. It should be investigated experimentally. There seems no practical way in which embryonated eggs, dried and floating in the air, can in daily life be prevented from reaching the respiratory mucosa and thereon, it must be concluded, hatching; the only feasible line of attack is to prevent their reaching the air at all, and here treatment has its place. Sewered privies cleanly kept are sure safeguards for the user. But to devise privies of demonstrable effectiveness and inoffensiveness, to provide them for millions of people of poor means, and to alter the habits of these so that they religiously use and clean them, is a task which will not be completed within the lifetime of any of us. Yet most emphatically this consideration in no way justifies complacent acceptance of the present position. It is clear that much intensive work on the conveyance and means of prevention of this infection is urgently needed.

THE TYPHUS GROUP OF FEVERS.

VAN MEIRHAEGHE (A.). Aperçu d'ensemble sur les fièvres exanthématiques attribuées au genre Rickettsia. [**Summary Outline of the Typhus-like Fevers of Rickettsial Origin.**]—*Rev. Belge Sci. Méd.* 1934. Jan. Vol. 6. No. 1. pp. 37–68. [143 refs.]

This paper is a review of our present knowledge and of recent research work on typhus and typhus-like fevers. The major part is taken up with a full account of epidemic typhus from the historical, clinical and etiological standpoints, a special paragraph being devoted to the Weil-Felix reaction. Other varieties of typhus are then discussed; these are divided up as follows:—(1) Typhus of the New World. Tabardillo and Brill's disease; (2) Rocky Mountain spotted fever; (3) Sao Paulo typhus; (4) Japanese River fever; (5) Boutonneuse fever; (6) "Mite" fever of Sumatra.

Recent work on these diseases is fully discussed on the same plan as in the first section dealing with true typhus. It is pointed out that probably varieties No. 3 and 6 are identical with Nos. 2 and 4 respectively. A very valuable bibliography is appended including no fewer than 143 papers referred to in the article. *D. Harvey.*

DO AMARAL (Afranio) & MONTEIRO (J. Lemos). Histoire naturelle et classification des rickettsioses. Position systématique du "typhus exanthématique de S. Paulo." [**Natural History and Classification of the Rickettsiases.**]—*Rev. Sud-Américaine de Méd. et de Chirurg.* Paris. 1933. Nov. Vol. 4. No. 11. pp. 781–817. With 2 diagrams. [55 refs.]

The authors discuss the various classifications which have already been proposed for the typhus group of diseases (fièvres exanthématiques) and suggest that they should be grouped under the name "Rickettsioses." They adopt the view of FLETCHER that the Rickettsia bodies were originally parasites of plants, as are certain flagellates, and suggest that these parasites adapted themselves in mites which suck the juices of the plants, these mites infected rodents on which they fed and in turn other ectoparasites of the rodents became infected and Rickettsia was carried to man by the mite, the tick, the flea, and the louse in that order.

They propose that the Rickettsiases should be grouped as follows:—

Group I. Diseases carried by the mite. Type.—Japanese River fever.

Group II includes the so-called "Tropical Typhus" of India, Africa and Malaya.

Group III. Tick-borne diseases. Type.—Boutonneuse fever.

Group IV endemic and epidemic typhus.

Group I.

Oriental Rickettsiasis.

1. Japanese type. *R. orientalis* Nagayo 1931
1a. Sumatra type ,, ,,

Group II.

Tropical Rickettsiasis.

1. Malaya type. *R. megawi*
1a. Australian type. ,,
1b. Indian type. ,,
1c. African type. ,,

Group III.

1.	Boutonneuse Rickettsiasis. Mediterranean	*R. conori.*
2.	Rocky Mountain Fever Western type	*R. rickettsi*
3.	Rocky Mountain Fever Eastern type	*R. typhi*
4.	Sao Paulo type	*R. brasiliensis*

Group IV.

1.	Brill's Disease	*R. muricola*
2.	Endemic Typhus	*R. mooseri*
3.	Trench Fever	*R. pediculi*
4.	Epidemic Typhus	*R. prowazeki*

Group II includes several types of fever the etiology of which has not yet been fully worked out; when this has been accomplished it would simplify matters if this group disappeared, types 1 and 1a being included in Group I and types 1b and 1c in Group III where they naturally belong.

[A separate name is given to each of the Rickettsias associated with the different types of the disease; this is confusing to the student; if viruses have been shown to be immunologically identical it would appear that the Rickettsia associated with these viruses could be given the type name. This would reduce considerably the number of such names, thus:

Group I. *R. orientalis*—mite diseases.
Group III. *R. rickettsi*—tick disease.
Group IV. *R. prowazeki*—flea and louse disease.] *D. H.*

Otto (R.). Flecktyphus und endemische Fleckfieber. [**Typhus and Endemic Spotted Fever.**]—*Zent. f. Bakt.* I. Abt. Ref. 1934. Mar. 22. Vol. 113. No. 5/6. pp. 138–144.

This paper is a review of recent investigations on typhus and the typhus-like fevers in the old and the new world. Practically all the papers referred to have already been reviewed in the *Bulletin*.

The author divides the typhus-like diseases into 3 groups:—

1. Louse typhus of the Old World, "Fleckfieber."
2. The milder typhus-like fevers of the New World (Brill's disease and Tabardillo) carried by the rat flea from rat and mouse to man.
3. Typhus-like fevers carried by the tick (American Rocky Mountain fever) or by the mite (tsutsugamushi fever).

The following differential table is also given:—

Epidemic Type.	*Endemic Type.*
(Louse) spotted fever	(Rat) spotted fever
Typhus exanthematicus	Febris exanthematicus
Source of infection.	
From man to man—by the louse.	From rat to rat by rat flea or rat louse. Occasionally from rat to man by rat flea.
Symptoms in man.	
Marked nervous involvement; petechiae	Slight or no nervous phenomena; rose spots; no petechiae

Epidemic Type.—cont.	*Endemic Type.*—cont.
Prognosis.	
Grave	Good usually
Season.	
Winter and spring	Mostly summer and autumn
Experimental animals.	
Guineapig.	
Nodules in brain; occasionally slight scrotal swelling	Nodules scanty in brain; marked swelling of scrotum and periorchitis is the rule
Rat.	
Inapparent infection; experimental passage of virus uncertain	Fever; experimental passage successful
Rickettsia.	
Difficult to find in experimental animals	Numerous in cells of the tunica in experimental animal.

D. H.

BADGER (L. F.). **Endemic Typhus of the United States.**—*Southern Med. Jl.* 1934. Feb. Vol. 27. No. 2. pp. 159–161.

The term "endemic" typhus is gradually replacing the name Brill's disease in America and elsewhere. This disease is immunologically identical with European typhus. It is apparently increasing in the States and, although rarely fatal, is a serious menace owing to the amount of incapacity it causes.

The vector is the rat flea and the reservoir is the rat; it is an urban disease and largely of coastal cities. The control of the disease should follow the lines of plague prevention—rat destruction and rat proofing of houses, shops, stores and ships. *D. H.*

LÉPINE (P.) & BILFINGER (F.). Le typhus murin est une maladie épidémique des rats. [**Murine Typhus an Epidemic Disease of Rats.**]—*Bull. Soc. Path. Exot.* 1934. Jan. 10. Vol. 27. No. 1. pp. 2–7.

The authors noted that when rats were examined during the winter 1932–33, when cases of endemic typhus were occurring in Athens, a large number of rats were found to be infective and strains of typhus were readily obtained from fleas captured on these rats. A year later, when no human cases were reported, a much larger number of rats were examined, but only very few were found to be infected; over 1,000 fleas were inoculated into guineapigs and only one strain of virus was obtained. Discussing these results the authors are of opinion that rat typhus is not an endemic disease of rats (the infection lingering on continually) but an epidemic disease with sudden outbursts, the rat population then becoming immune and the virus disappearing, the disease only reappearing when a new and non-immune rat population is established; if the virus is then reintroduced another outburst will occur. After the epidemic outbursts a positive Weil-Felix reaction is found in many of the rats. *D. H.*

ISABOLINSKI (M. P.), SOBOLEWA (R. M.), STRATANOWITSCH (N. J.), RIWKINA (S. L.) & MOSKALEWA (T. A.). Zur Frage der epidemiologischen Bedeutung der Weil-Felix-Reaktion bei Flecktyphus. [**The Bearing of the Weil-Felix Reaction on the Epidemiology of Typhus Fever.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1934. Feb. 15. Vol. 81. No. 5/6. pp. 405–409. [Summary appears also in *Bulletin of Hygiene.*]

The Weil-Felix reaction was found to be positive in sera from 117 out of 1,097 healthy persons examined. Of these 117 sera, 38 came from persons who had suffered from typhus fever within the previous two years. The remaining 79 sera, constituting 7·2 per cent. of the whole, came from persons who had no history either of typhus or of contact with it. In this group the titres varied from 1/50 to 1/200, the commonest titre being 1/75.

Sera were also examined from 103 members of the medical personnel serving in the infectious division of the No. 1 Soviet hospital in Smolensk. Apparently 56 of these sera reacted positively, the commonest titre being 1/400. [The figures in the text are discrepant.] The majority of these positive sera came from persons with no history of typhus fever. The blood of 8 persons reacting at 1/400 was inoculated in 3 cc. quantities intraperitoneally into guineapigs. Three of the animals became febrile on the 17th day and one on the 20th day, the temperature lasting for 5 or 6 days. Normal guineapigs inoculated from 3 of these animals likewise developed fever—this time after an incubation period of 6–7 days. It is interesting to note that one of the persons whose blood had been inoculated into a guineapig developed typhus fever. [This patient became ill either 8 days or some weeks after the blood had been examined; the text is not clear.] This suggests that healthy carriers of the typhus virus may occur amongst those in contact with patients.

In view of the fact that 7 per cent. of sera from healthy persons who had never been in contact with typhus fever agglutinated Proteus X19, the authors regard the Weil-Felix reaction as of limited value in epidemiological studies. *G. S. Wilson.*

APPEL. La lutte contre le typhus exanthématique dans le département de Constantine. Quatre années d'observation-déductions pratiques. [**Four Years of Anti-Typhus Measures in Constantine.**]—*Rev. Méd. et Hyg. Trop.* 1934. Jan.–Feb. Vol. 26. No. 1. pp. 35–62.

There are many cases of typhus every year in this district of Algeria; the disease as a rule is mild in the native of the country but severe in the European; the author suggests as explanation in the one case an acquired or hereditary immunity, in the other too severe medication!

Although the disease does not occasion many deaths it is a serious cause of disability. It is a disease of the winter, clothes are never removed and baths not taken, lice are plentiful and infective louse excreta contaminate the skin. Influenza and bronchitis complicate the situation and famine causes movement of the people and crowding in certain places.

The disease usually appears first in the southern regions and spreads north; certain areas are endemic centres; every year it breaks out in these districts in the same villages and even the same houses.

The available transport for dealing with the disease is one Citroen ambulance and one ½-ton Citroen lorry to carry materials for disinfection. The campaign is carried out under 3 headings—(*a*) Search for cases; (*b*) Isolation of cases and contacts; (*c*) Disinfection. Cases are exceedingly difficult to find as there is concealment of the disease and many roads are impassable for wheeled traffic; villages are remote.

If a number of cases are detected in one village a sanitary section arrives and the clothing of the entire village is disinfected house by house by means of sulphur gas (owing to scarcity of water steam is not available); special cloaks are provided for the people while their clothes are being disinfected; or the clothes are disinfected in two lots. Isolation of cases is carried out in tents or a special house taken over for the purpose.

A special section of the paper deals with typhus among the nomadic peoples who come into the district from the south every year along the same routes and camp in the same places, and invariably bring typhus with them. Recommendations are given for dealing with the disease among these nomads and as regards provision for improved materials and more personnel for combating typhus. *D. H.*

Des Essarts (J. Quérangal). Au sujet d'un nouveau cas de typhus endémique bénin observé sur un navire de guerre, au port de Brest. [**A Fresh Case of Endemic Typhus on a Warship at Brest.**] —*Bull. Soc. Path. Exot.* 1934. Feb. 14. Vol. 27. No. 2. pp. 108–111.

A typical case of endemic typhus with a very marked maculopapular rash which involved the palms and soles. The Weil-Felix reaction was positive in a dilution of 1/6,000.

The interesting point is that the case occurred in the cruiser "Diderot" which had been laid up in the harbour at Brest for three years and no cases of typhus fever have been known to occur during these years in this port. Blood taken from the patient at the height of the fever and inoculated into a guineapig gave the typical reaction of rat typhus virus, *i.e.*, fever and marked swelling of the scrotum.

D. H.

Lemierre (A.), Layani (E.) & Pham-Huu-Chi. Sur un cas isolé de typhus bénin. [**A Sporadic Case of Endemic Typhus.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1934. Feb. 12. 50th Year. 3rd Ser. No. 4. pp. 178–185. With 1 chart.

An isolated case of endemic typhus in the suburbs of Paris.

The disease commenced on 17th September 1933 with rigor and sweating and intense, persistent headache. Eight days later a profuse macular rash appeared which spread over the body and involved the palms and soles. Blood cultures (twice) were negative and also the Widal reaction. On the 29th of September the patient's serum gave a positive Weil-Felix reaction in a dilution of 1/1,000 and later of 1/500. It was discovered that the patient had had typhus fever (epidemic) in Russia in 1919 but his servant who also had typhus in Russia at the same time gave a completely negative Weil-Felix reaction. *D. H.*

FENNEL (Eric A.). **Endemic Typhus Fever in Hawaii.**—*Jl. Amer. Med. Assoc.* 1934. Apr. 7. Vol. 102. No. 14. pp. 1135–1136.

The author describes a typical case of endemic typhus which gave a positive Weil-Felix reaction in a dilution of 1/10,000 with Proteus X19. He is of opinion that there have been in the past a number of such cases in Honolulu which have been diagnosed as typhoid fever. The sera of 3 such cases (fever 2 years ago) were tested and gave positive W.-F. reactions in dilutions of 1/320, 1/640 and 1/1,280. Up to date about 10 cases of typhus have been detected in Honolulu and are due, the author considers, to infection from rats. *D. H.*

BABALIAN (A.). Seize cas de typhus exanthématique traités avec succès par l'autohémothérapie. [**Sixteen Cases of Typhus treated with Success by Autohaemotherapy.**]—*Bull. Soc. Path. Exot.* 1934. Mar. 14. Vol. 27. No. 3. pp. 235–236. With 3 charts.

15 cc. of blood was drawn off from the patient and injected; marked general improvement was noted and an early termination of the fever.

D. H.

HESCHELES (I.) & FLECK (L.). Ueber die Eigentümlichkeiten der Exanthin- (Fleckfieberhaut-) Reaktion beim Menschen. [**Characteristic Skin (Exanthin) Reaction of Proteus Extract in Man.**]—*Ztschr. f. Immunitätsf. u. Exper. Therap.* 1933. July 20. Vol. 79. No. 5/6. pp. 514–520. With 2 figs.

The injection of this fluid into the skin of adults who have not had typhus gives rise to a marked cutaneous reaction, but only in about 50 per cent. of small children and 75 per cent. at school age.

In adults the reaction continues positive during the course of other fevers, *e.g.*, typhoid, relapsing fever, etc., but after the 5th to 7th day becomes negative in typhus cases. The course of the "exanthin" reaction was followed in 3 people during and after immunization with Weigl's Rickettsia vaccine; all were strongly positive before inoculation but became negative later when they developed a positive Weil-Felix reaction. *D. H.*

MOOSER (H.), VARELA (Gerardo) & PILZ (Hans). **Experiments on the Conversion of Typhus Strains.**—*Jl. Experim. Med.* 1934. Feb. 1. Vol. 59. No. 2. pp. 137–157. [25 refs.]

The authors have noticed that strains of typhus virus isolated from cases of fever in Mexico in long standing epidemics give the same reactions in experimental animals as do strains of the Old World typhus virus, *i.e.*, inapparent infection in rats and fever without scrotal swelling in guineapigs. The present paper is concerned with the transformation of such strains into typical rat typhus strains.

The authors had observed that Rickettsia in lice and fleas multiply in the cells lining the alimentary canal and always in close and frequent contact with fresh blood; also in experimental animals these germs are found in the cells lining blood vessels and in blood plasma in the scrotal sac. The Rickettsia of epidemic typhus fever (Old World) are specially haemophilic. With this in mind rats were inoculated intraperitoneally with the virus and injections of fresh blood were made daily into the peritoneum; it was found that Rickettsia multiplied much more rapidly in animals so treated. By means of this

" blood " method it has been found possible to change these epidemic strains into murine strains; that is to say after several passages through rats with blood added, these strains produce severe fever in rats and fever and scrotal reaction in guineapigs; if only passaged through a few rats the strains may revert but after several passages they become fixed. A Tunisian strain of typhus virus from NICOLLE'S laboratory when passaged in this manner also developed the same properties as the rat typhus virus.

Mooser has always been of opinion that the rat typhus virus is the original strain and that the epidemic virus results from the long passage of typhus virus through man-louse-man; the rat is the reservoir and inter-epidemic source of the virus and when passaged through the rat the virus again acquires the properties of the murine virus.

It has been suggested that the epidemic virus may be kept alive by means of mild unrecognized cases of the disease in man but Mooser and his co-workers point out that it is difficult or impossible to infect lice from such mild cases and that lice die of the infection whereas the rat flea does not. The rat is the reservoir of both the endemic and epidemic virus. *D. H.*

DYER (R. E.). **Effect of Flea Passage on Epidemic Typhus Virus.**—*Public Health Rep.* 1934. Feb. 16. Vol. 49. No. 7. pp. 224–225.

MOOSER and others have claimed that if the virus of epidemic typhus be passed through the rat flea it produces in guineapigs a similar reaction to that of the endemic virus. The author was unable to produce a change of type.

The author obtained a strain of epidemic virus from BREINL and passed this through rat fleas; these insects were allowed to feed on infected rats, then collected and crushed up and injected into guineapigs. The first and second passages produced no change whatever in the action of the virus (no testicular swelling), the 3rd passage strain also showed no change until it became contaminated with *S. enteritidis* (Badger) and guineapigs having the cross infection with this organism showed scrotal lesions which, grossly, could not be differentiated from those caused by endemic typhus virus. *D. H.*

GRÜNFELD (A. A.), SEREBRJANNAJA (A. I.) & NEUMANN (M. W.). Experimentelle Studien ueber das Flecktyphusvirus. [**Experimental Studies on the Typhus Virus.**]—*Zent. f. Bakt.* I. Abt. Orig. 1933. July 11. Vol. 129. No. 1/2. pp. 56–69. With 7 figs. [11 refs.]

The virus employed in this research was obtained from the blood of cases of the disease taken during the period from the 7th to the 12th day of fever. The blood was inoculated intraperitoneally into guineapigs in doses ranging from 2 to 4 cc. In two instances positive results were obtained and the virus was studied by passage through a series of guineapigs.

In addition to the characteristic febrile reaction in the guineapigs the following symptoms had also to be present before a positive result was returned.—1. Loss of weight. 2. A monocytosis. 3. Typical

typhus nodes in the brain and other organs, and also a sterile blood culture.

A very complete table is given showing 16 passages of the virus through guineapigs with the incubation periods, days of fever and presence of nodes, weight loss and monocyte counts. Cell counts of several infected guineapigs are given in graphic form.

Twenty-one rats were inoculated from guineapigs but only 3 reacted with fever; in one of these at post-mortem typical nodes were found in the brain. An emulsion of the brains of 5 of the rats which had not developed fever was made and inoculated into guineapigs; in one of these at post-mortem nodules were found in the brain. Rabbits were also inoculated with the virus in the testicle and it was found that it could be passaged in this manner and that this is a useful method for preserving the virus *in vivo*, up to 23 days in one instance.

D. H.

LÉPINE (P.) & BILFINGER (F.). Infection expérimentale du pou par le virus murin du typhus exanthématique. [**Experimental Infection of the Louse by Murine Typhus.**]—*C. R. Acad. Sci.* 1934. Apr. 23. Vol. 198. No. 17. pp. 1553–1555.

Monkeys infected with European rat typhus virus develop a very mild type of fever and lice fed on these monkeys do not become infected. But by reducing the resistance of the monkeys by exposure to cold together with injections of India ink, a more severe disease develops and lice (*P. corporis*) fed on these monkeys show Rickettsia in the intestine about the 7th day, and become infective for guineapigs from the 10th to 16th day. The infection of lice with rat typhus virus from monkeys is another point in favour of the identity of the typhus viruses, endemic and epidemic. *D. H.*

LAIGRET (Jean) & DURAND (Roger). Conservation des virus exanthématiques à basse température. [**Preservation of Typhus Virus at Low Temperatures.**]—*Arch. Inst. Pasteur de Tunis.* 1933. Dec. Vol. 22. No. 4. pp. 499–504.

Typhus viruses die out rapidly at ordinary room temperatures and only survive for a few days at 0°C. but the authors have found that if kept at a temperature of −10°C. to −12°C. they survive for at least 20 days. Brains of infected guineapigs were placed in a Frigidaire at this temperature and the virus could be recovered up to 20 but not after 30 days. *D. H.*

SILBER (L. A.) & DOSSÈRE (E. M.). Culture des virus du typhus exanthématique. [**Culture of Typhus Virus.**]—*Arch. Inst. Pasteur de Tunis.* 1933. Dec. Vol. 22. No. 4. pp. 486–490.

—— & ——. Ueber Züchtung filtrierbarer Virusarten auf nichtpathogenen Mikroben. III. Mitteilung: Kultivierung des Flecktyphusvirus.—*Zent. f. Bakt.* I. Abt. Orig. 1934. Apr. 5. Vol. 131. No. 3/4. pp. 222–232. With 12 figs.

The authors review previous research and point out that so far all workers have utilized living cells in their medium for the culture of Rickettsia. They note that Rickettsia multiplies rapidly in the gut

of the louse along with numerous saprophytic bacteria. They therefore inoculated flasks of broth with torula and sarcina and with small quantities of blood taken from patients at the height of an attack of typhus or else small portions of the brain of infected guineapigs. The cultures were incubated at 30°C. for 8 days. By this method they were able to passage the virus through at least 8 generations. Temperature charts are shown, demonstrating the reactions in guineapigs after inoculation with these cultures. Cultures from the tissues of these animals proved sterile and the virus was passed on to other animals which reacted in a typical manner. Typical typhus lesions were demonstrated in the brains of the infected animals and microphotographs are given of these and also other photographs showing numerous Rickettsia bodies in the protoplasm of the cells of the tunica vaginalis of guineapigs infected by the 8th generation of culture, and from guineapigs passaged from these.

Rabbits inoculated with the culture virus developed a positive Weil-Felix reaction although they showed no other signs of infection. Lice were inoculated by the rectum with small amounts of the culture and killed after a period of 4–6 days; numerous Rickettsia bodies were demonstrated in the cells lining the alimentary canal.

The authors remark that this method of employing bacterial cells in place of tissue cells may be found useful in the cultivation of other viruses besides Rickettsia. *D. H.*

KLIGLER (I. J.) & ASCHNER (M.). **Cultivation of European Type of Typhus Rickettsia in Presence of Live Tissue.**—*Proc. Soc. Experim. Biol. & Med.* 1933. Dec. Vol. 31. No. 3. pp. 349–351.

The intestines of lice, infected with the European strain of typhus virus, were removed aseptically and placed in a drop of saline solution on a sterile slide. Normal guineapig tunica tissue was macerated in the fluid and allowed to stand for 15 minutes; small amounts of this were then placed in 3 cc. Tyrode serum and incubated at 30°C. for 8 days. When examined numbers of Rickettsia were found in the cells and also free in the fluid. A successful subculture was made and proved to be infective for a guineapig. The strain was passaged. *D. H.*

FEJGIN (B.) & SPARROW (H.). Au sujet de quelques microorganismes, isolés des organes de cobayes et rats infectés par le virus typhique murin de Mexico. [**On Bacteria isolated from the Organs of Guineapigs and Rats infected with Rat Typhus Virus of Mexico.**] —*Arch. Inst. Pasteur de Tunis.* 1933. Dec. Vol. 22. No. 4. pp. 477–485.

Guineapigs and rats were inoculated with Mexican virus; the former were killed on the first day of fever, the latter about the 8th day after inoculation when the Weil-Felix reaction was positive. The organs and blood of these animals were used for cultivation experiments.

In 7 cases a gram positive bacillus, diphtheroid, was isolated from the guineapigs. In 5 cases a motile Proteus bacillus, which did not produce indole, was isolated; this bacillus was of the X19 type and was agglutinated by the serum of rabbits which also agglutinated cultures of X19. *D. H.*

NICOLLE (Charles). Sur les conditions de la recherche des infections inapparentes chez les animaux qui ne réagissent pas visiblement à l'inoculation du virus d'une fièvre exanthématique ou d'un produit dans lequel on suppose sa présence. [**On the Conditions of Research into Inapparent Infections in Animals which have not shown any Symptoms after Inoculation with the Virus of one of the Typhus Fevers or of a Product in which the Presence of such a Virus is suspected.**]—*Arch. Inst. Pasteur de Tunis.* 1934. Mar. Vol. 23. No. 1. pp. 19–31.

Professor Nicolle apologizes for the prolixity of his title but explains that to abridge it in any way might obscure the exact meaning.

It is now generally agreed that in typhus research inapparent infections do frequently occur. There are two methods of confirming an inapparent or symptomless infection in animals.

(1) *The direct method.*—After injection of the virus or material which is suspected of containing the virus the usual incubation period is allowed to elapse; heart blood is drawn off from the animal at the time when the fever would be at its highest point in the usual course, and is injected into other guineapigs; if these animals react typically the result is positive and we still have the original animal alive for further test. A still more certain method is to kill the original guineapig and to inject emulsion of the brain into other animals. The original animal is however no longer available.

(2) *The indirect method.*—The animal which has not reacted must be kept until the 20th to 30th day after inoculation and then tested for immunity with a known typhus virus of fixed virulence which produces fever regularly in guineapigs. The recently isolated strains of rat typhus virus cannot be relied on in this respect. When employing this method a sharp distinction should be drawn between inoculation with a known typhus virus and inoculation with a substance which may or may not contain a typhus virus. In the first instance the indirect method may be sufficient, in the second only the direct method should be relied upon.

Instances of the correct and incorrect methods of carrying out such tests are given. *D. H.*

RONSE (Marguerite). Adaptation du virus du typhus murin aux Lérots et aux Hérissons. [**Adaption of Murine Typhus Virus to Dormice and Hedgehogs.**]—*C. R. Soc. Biol.* 1934. Vol. 115. No. 7. pp. 754–756.

The author inoculated several dormice and found that they were susceptible to the virus of rat typhus. These animals did not suffer in any way and had no fever but their brains proved to be infective for guineapigs and the virus was passed in series through several of these small rodents. In one instance a positive Weil-Felix reaction was noted. The hedgehog was also shown to be susceptible and gave a positive Weil-Felix reaction. *D. H.*

COMBIESCO (D.). Réaction de Weil-Félix chez les chiens de Constantza. [**Weil-Felix Reaction in Dogs at Constantza.**]—*C. R. Soc. Biol.* 1934. Vol. 115. No. 6. pp. 672–673.

Constantza is at present the only place in Rumania where boutonneuse fever is met with, 34 cases in 1931, 3 or 4 in 1933. Many infected

ticks were found in various parts of the town in 1932 but only one human case; the author considers that the virulence of the disease may be lowered by the immunity of the local dogs on which these ticks feed.

The serum of 43 dogs was tested; a strain of OX19 was employed; 19 of the sera gave a positive reaction, 1/50 or more, the highest titre being 1/500. Of the sera of 30 dogs in Bucharest where no cases of the fever have occurred none gave a positive reaction. *D. H.*

i. Combiesco (D.), Popesco (C.) & Vantu. Typhus exanthématique expérimental chez le chien. [**Experimental Typhus in the Dog.**]—*C. R. Soc. Biol.* 1934. Vol. 115. No. 9. pp. 996–998.

ii. ——. Réaction de Weil-Felix chez les chiens de Bessarabie. [**Weil-Felix Reaction in Dogs of Bessarabia.**]—*Ibid.* pp. 999–1000.

i. The authors have already shown that the dog is susceptible to the virus of typhus, both epidemic and endemic [see this *Bulletin*, Vol. 30, p. 891]. They now find that the virus can be passaged in these animals.

Dogs were inoculated intraperitoneally with an emulsion of the brain of infected guineapigs. The virus was passed through three series from dog to dog, and guineapigs inoculated from them gave a typical reaction. The serum of the dogs also showed a positive Weil-Felix reaction.

ii. The sera of 38 dogs were examined, from houses where cases of typhus fever had recently occurred. Two of these sera agglutinated OX19, one up to a dilution of 1/500 and one to 1/200; the other sera were negative, as also was agglutination with OX2; whereas in areas where boutonneuse fever occurred the sera of dogs agglutinated this strain as well as OX19. *D. H.*

Blanc (Georges), Noury (M.) & Baltazard (M.). Sensibilité de l'ecureuil de Gétulie *Xerus* (*Atlantoxerus*) *getulus* au virus du typhus murin de Casablanca. [**The Getulie Squirrel Sensitive to the Virus of Murine Typhus in Morocco.**]—*C. R. Soc. Biol.* 1934. Vol. 115. No. 1. pp. 8–9.

This small rodent found in Morocco closely resembles the spermophile (Citillus) which has already been shown to be susceptible to the virus of boutonneuse fever and also to typhus virus. Great difficulty was experienced in keeping these animals alive in captivity but sufficient work was done to show that they are susceptible to the rat typhus virus and guineapigs were successfully inoculated from them.

D. H.

Nicolle (Charles) & Laigret (J.). Faible sensibilité d'une chauve-souris (*Vespertilio kuhli*) à certains virus exanthématiques. [**Susceptibility of Bats to Typhus Virus.**]—*Arch. Inst. Pasteur de Tunis.* 1933. Dec. Vol. 22. No. 4. pp. 491–498.

Bats are difficult to keep in captivity and require an enormous number of insects for food. A few young bats can be kept healthy if fed on milk. It was found that hibernating bats could be utilized if kept in the dark at a low temperature. These bats were inoculated with the virus and killed about the 12th day and emulsion of the

brain was inoculated into other bats and into guineapigs as test indicator animals. Positive results were obtained with the Mexican typhus virus and with Rocky Mountain fever but could not be passaged a second time. The susceptibility of these bats is therefore only slight.

D. H.

KRITSCHEWSKI (I. L.) & SOLOWIOW (N. N.). Das Fleckfieber bei den wilden Ratten in Moskau. II. Mitteilung: Die Weil-Felix-Reaktion als Methode zur Feststellung des Flecktyphus bei Ratten. [**Typhus in Wild Rats in Moscow. The Weil-Felix Reaction as a Means of detecting Typhus in Rats.**]—*Zent. f. Bakt.* I. Abt. Orig. 1934. Apr. 5. Vol. 131. No. 3/4. pp. 232–235.

The sera of 103 wild rats were tested against emulsions of Proteus X19 and 28 per cent. gave a positive reaction, that is in dilutions of 1/10 up to 1/500. Six of those which gave positive reactions were killed and the brains emulsified and injected into guineapigs; in one case a positive reaction was obtained, *i.e.*, fever and orchitis. [No mention is made of the presence of Rickettsia or proof of immunity by injection of a known typhus virus.] It is remarked that in the rats which did not infect, the positive Weil-Felix reaction was probably due to a previous attack of typhus in the rat.

The sera of 70 white rats kept in the Institute were then tested and 41 per cent. of these reacted positively in dilutions of 1/10 up to 1/200. One rat (1/200 positive) was killed and an emulsion made of the brain and injected into a male guineapig; after an incubation period of 13 days this animal developed fever and also orchitis. Five white rats (negative Weil-Felix) were inoculated with the virus of rat typhus, after 14 days the sera were tested and all but one gave a positive reaction 1/300; one of these rats was then killed and the brain emulsion inoculated into two guineapigs, both developed fever reaction.

D. H.

SUZUKI (K.). Untersuchung ueber Rickettsia-Infektion (sogenanntes Rattenfleckfieber-Virus) und Weil-Felix-Reaktion bei Ratten in Hamburg. [**Rickettsia Infection and Weil-Felix Reaction in Rats in Hamburg.**]—*Zent. f. Bakt.* I. Abt. Orig. 1934. Apr. 5. Vol. 131. No. 3/4. pp. 236–240. [16 refs.]

Ten wild rats were captured in the port of Hamburg, one (*Mus rattus*) on board ship, 9 (*Mus norvegicus*) from various districts in the town.

Five of these rats gave a positive Weil-Felix reaction 4 with X19 and 1 with OX19 (*sic*). All 10 rats were killed and the brain emulsion inoculated into male guineapigs. Three of these gave a positive reaction. It is stated that in smears from the tunica vaginalis Rickettsia were found in some of the infected guineapigs but none of them were tested for immunity against a known virus. *D. H.*

NICOLLE (Charles) & SPARROW (Hélène). Existence d'un virus typhique chez les rats de Tunis. Caractère de ce virus. [**Characters of a Typhus Virus from Tunis Rats.**]—*C. R. Acad. Sci.* 1934. Apr. 9. Vol. 198. No. 15. pp. 1334–1336.

There are two methods of demonstrating the virus of a disease such as typhus in wild rats; the one is to inject into susceptible

laboratory animals an emulsion of the brains of several rats, the second to inject the emulsion of the brain of one rat at a time. Employing only the first method one is apt to get confusing results due to the presence of several different pathogenic agents in the group of rats.

The authors employed both methods and succeeded in isolating the typhus virus from the wild rats of Tunis by each. In the present note only the results obtained by the first method are detailed.

The rats were placed in groups of 5 and emulsions of the brains were, in each group, injected into 2 guineapigs. In all 174 wild rats were examined and 70 guineapigs were used in the tests. Five lots of 5 rats had been tested when the tests had to be abandoned owing to an outbreak of Paratyphosus B infection among the laboratory guineapigs. In two instances the virus of typhus was isolated from rats ; one strain was passaged 15 times and the other 10 times. Virus No. 1 when inoculated into white rats produced a short fever which was fatal in 25 per cent. of the animals ; the serum of 50 per cent. of these rats gave a positive Weil-Felix reaction and also agglutinated the Rickettsia of epidemic typhus and of Mexican typhus. In guineapigs this virus gave rise to fever and also produced a marked swelling of the scrotum in all. Seven of the guineapigs which had had fever following injection of the Tunis rat virus were later tested with the virus of " historical " typhus virus and 6 of them proved to be immune ; it was also shown that the Tunis rat virus protected guineapigs against the Toulon rat typhus virus. Out of 545 wild rats tested the serum of 3·5 per cent. gave a positive Weil-Felix reaction ; but of the 5 rats composing the group from which virus No. 1 was isolated none gave a positive Weil-Felix reaction. *D. H.*

NICOLLE (Charles). L'existence du typhus murin chez les rats de la région parisienne reste toujours à démontrer. [**Does Murine Typhus exist in Paris Rats ?**]—*Bull. Acad. Méd.* 1934. Feb. 27. 98th Year. 3rd Ser. Vol. 111. No. 8. pp. 299–304.

In 1932 BRUMPT stated that he had been able to demonstrate the presence of the virus of typhus in the brains of rats captured in Paris and in the suburbs but only in one instance. [This *Bulletin*, Vol. 29, p. 773 ; *ante* p. 240.]

Professor Nicolle in 1933 examined the brains of 146 wild rats from the same localities but was not able to isolate the typhus virus ; he is of opinion, as the title of this discussion suggests, that this virus has not yet been isolated in Paris.

BRUMPT refers to the work of LÉPINE in Athens, who showed that in the year 1932 the typhus virus (murine) could be easily obtained from the brains of rats caught in the city and also from fleas caught on these rats ; but a year later over 400 rats had to be examined before the virus was found and more than 1,000 fleas. *D. H.*

NICOLLE (Charles), GIROUD (Paul) & SPARROW (Hélène). Présence exceptionnelle du virus murin dans les urines des rats infectés expérimentalement par ce virus. [**The Occasional Presence of Typhus Virus in the Urine of Rats Experimentally Infected.**]—*C. R. Acad. Sci.* 1934. Jan. 29. Vol. 198. No. 5. pp. 414–416.

A few drops of the urine of infected rats were instilled into the eye of guineapigs ; 7 out of 21 developed fever but only one of these

proved to be immune when tested later with a known typhus virus. A similar result—positive in one case—followed when the urine was injected under the conjunctiva; but no reaction was obtained when it was inoculated subcutaneously or intraperitoneally. *D. H.*

NICOLLE (Charles), GIROUD (Paul) & SPARROW (Hélène). Présence exceptionnelle du virus typhique murin dans les urines des rats, infectés expérimentalement par ce virus. [**Exceptional Presence of Typhus Virus in Experimentally Infected Rats Urine.**]—*Arch. Inst. Pasteur de Tunis.* 1934. Mar. Vol. 23. No. 1. pp. 1–14.

Professor Nicolle again draws attention to the fact that when the organs or urine of wild rats is injected into guineapigs there are other germs than the typhus virus which may produce fever and even fever with orchitis in these animals. The presence of the typhus virus should only be considered as proved if certain tests are successfully carried out. The most important of these tests is (*a*) the presence of Rickettsia in the cells of the tunica and (*b*) a definite immunity to a test dose of a *known* typhus virus.

Three strains of rat virus were utilized in the present series of experiments, one a Mexican strain, the others from Toulon. Three methods of application were used: (*a*) The urine of infected rats was instilled into the conjunctiva of guineapigs and kept in contact for 8 minutes; (*b*) the urine was injected under the conjunctiva; (*c*) the urine was injected intraperitoneally. The urine of 93 rats was tested and of these only 2 proved positive, both with the Mexican virus, one by instillation, the other by subconjunctival injection, none by the intraperitoneal route. Seventy-four rats were infected with the Mexican virus and 19 with the European rat virus (none of these gave a positive reaction).

Although it is obvious from the results of these experiments that the amount of typhus virus in the urine of rats is very minute, still the possibility of infection by this route should be kept in mind, especially by those handling infected rats. *D. H.*

GAJDOS (E.) & TCHANG (J.). Le gonflement scrotal du cobaye dans le typhus exanthématique expérimental de Chine. [**Scrotal Swelling of Guineapigs in Experimental Typhus in China.**]—*Arch. Inst. Pasteur de Tunis.* 1934. Mar. Vol. 23. No. 1. pp. 37–42.

Two strains of typhus virus are maintained in the Peking laboratory, both from cases of the disease in man, one from a Chinese in Mongolia and one from a European in Peking.

Both these strains have already been shown to produce fever and swelling of the scrotum when inoculated into guineapigs. The scrotal reaction appears on or about the first day of the fever, lasts for 3 or 4 days and then completely disappears. Rickettsia were not discovered in the fluid from the swollen scrotum but at post-mortem when smears were made from the inflamed tunica and stained Rickettsia were readily demonstrated. The scrotal reaction did not appear in all infected guineapigs; with virus N about 50 per cent. were positive, with virus P about 30 per cent. After a certain number of passages the reaction becomes less and less and finally is only occasionally seen, and when it does occur is much milder in character, the febrile

reaction however remaining as before. This change in the scrotal reaction occurred at the 14th passage with strain N and at the 15th passage with strain P; the reaction completely disappeared after the 37th passage in both cases. *D. H.*

D'AUNOY (Rigney) & FINE (Archie). **Influence of Rabic Virus on the Agglutination of** *Proteus* X19 **Organisms.**—*Jl. Trop. Med. & Hyg.* 1934. Mar. 1. Vol. 37. No. 5. pp. 65–66.

It has been stated that severe cases of typhus with pronounced nervous symptoms may simulate rabies. The authors tested the serum of rabbits, which were suffering from rabies due to fixed and street virus, against Proteus X19 but none of the sera gave a positive reaction. The sera of patients who were undergoing or had just undergone prophylactic inoculation for rabies were also tested but all gave a negative Weil-Felix reaction; as did the sera of two men who were actually suffering from rabies. *D. H.*

ZINSSER (Hans) & CASTANEDA (M. Ruiz). **Active and Passive Immunization in Typhus Fever.**—*Proc. Nat. Acad. Sci.* 1934. Jan. Vol. 20. No. 1. pp. 9–11.

—— & ——. **Studies on Typhus Fever. XII. The Passive Immunization of Guinea Pigs, infected with European Virus, with Serum of a Horse treated with Killed Rickettsia of the Mexican Type.**—*Jl. Experim. Med.* 1934. Apr. 1. Vol. 59. No. 4. pp. 471–478. With 3 charts.

In a previous paper the authors showed that the serum of a horse, immunized by killed Rickettsia of Mexican typhus, protected guineapigs against the homologous virus but not against the virus of European typhus [this *Bulletin*, Vol. 30, p. 887]. However, they now show that if the serum is given 3 or 4 days after the dose of virus then there is abundant evidence of protection against the European virus also. Their experiments show that the serum of a horse treated with Mexican Rickettsia acquires a Weil-Felix reaction, agglutinates the European louse vaccine and protects against the European virus. *D. H.*

NICOLLE (Charles), LAIGRET (Jean) & SPARROW (Hélène). Vaccination contre les typhus exanthématiques par voie digestive chez le singe. [**Vaccination of Monkeys against Typhus by the Digestive Route.**]—*C. R. Acad. Sci.* 1933. Dec. 26. Vol. 197. No. 26. pp. 1709–1711. Also in *Arch. Inst. Pasteur de Tunis.* 1934. Mar. Vol. 23. No. 1. pp. 15–18.

An attempt was made to immunize monkeys against typhus virus by feeding them on the brains of infected guineapigs. Three strains of virus were employed, a rat typhus virus, a true typhus virus, and a virus of Rocky Mountain fever. Of 8 monkeys which were fed on typhus infected brains 4 proved to be immune when subsequently tested. No immunity was produced in the case of Rocky Mountain fever. Incidentally it has been shown in two instances that the ingestion of the brain of guineapigs infected with rat typhus virus is innocuous for man. *D. H.*

VARELA (Gerardo) & PARADA GAY (Miguel Angel). Préparation du vaccin contre le typhus exanthématique. [**Preparation of Vaccine against Typhus.**]—*C. R. Soc. Biol.* 1934. Vol. 115. No. 13. pp. 1465–1466.

The authors employ the method of MOOSER to obtain large numbers of Rickettsia. Rats are inoculated intraperitoneally with the testicular washings from infected guineapigs and injections of fresh blood are made at the same time and daily for 4 or 5 days. Large numbers of Rickettsia are found in the cells lining the peritoneal cavity of the rat and also free in the exudate. The fluid from the peritoneum and scrapings from the wall are collected and emulsified in 2 per cent. formolized citrate solution; this is centrifuged and the precipitate washed several times and finally triturated in a mortar and suspended in 0·2 per cent. formolized citrate solution. The vaccine is standardized by staining the fluid and noting the number of Rickettsia per cc.

D. H.

TZEKHNOWITZER (M. M.) & PALANT (B. L.). Die Neurovakzine bei Flecktyphus im Experiment. [**Neurovaccine in Experimental Typhus.**]—*Zent. f. Bakt.* I. Abt. Orig. 1933. July 11. Vol. 129. No. 1/2. pp. 69–80.

The authors refer to the work of NICOLLE & SPARROW, who attempted to protect animals and man by means of a living vaccine (emulsion of the brain of infected guineapigs).

The authors prepared a vaccine on the same lines from local strains of typhus virus and the minimal lethal dose for guineapigs was determined. Three trials were made on guineapigs with this vaccine, one with living vaccine, one with vaccine killed by carbolic, and one with vaccine killed by formalin. Of the living vaccine only one dose was given but with the others four at intervals. The best results were obtained with the formalin killed vaccine; out of 8 immunized guineapigs only one developed fever when tested one month later, whereas 3 controls all contracted fever. As a further control 8 guineapigs were given emulsion of brain of normal guineapigs; 4 received 4 doses and 4 ten doses. When tested one month later all developed fever, thus showing that the protection afforded by the vaccine is due to a specific antigen.

D. H.

FLETCHER (William). Typhus tropical et maladies de la même famille. [**Tropical Typhus and Diseases of the Same Group.**]—*Bull. Office Internat. d'Hyg. Publique.* 1934. Jan. Vol. 26. No. 1. pp. 95–110. [64 refs.]

A report of these typhus-like diseases was submitted to the Permanent Committee of the Office International about 4 years ago and the present report brings the subject up to date.

The report is divided into sections. The first dealing with the classification of the diseases, another with typhus in rats and rat fleas and another with Rickettsia in association with the virus in animals and in insects. The present views in regard to the Weil-Felix reaction are given and also a resumé of recent researches in British Colonies. The reporter is now inclined to the view that "scrub typhus" of Malaya is identical with Japanese River fever and that "shop typhus" is endemic typhus or Brill's disease; the first carried by a larval mite,

a common parasite of rats in the palm oil and rubber plantations; and the second by the rat flea, *X. cheopis*, a common parasite of rats in the shops in towns and especially in grain stores. *D. H.*

PORTELLY (J.). **A Review of Tropical Typhus in Negri Sembilan.**—*Malayan Med. Jl.* 1933. Dec. Vol. 8. No. 4. pp. 253–256.

A series of 84 cases of tropical typhus was reported in Negri Sembilan over the period February 1930 to August 1933.

Only 15 of these cases were definitely diagnosed as of the W or urban type, the others were of the K or scrub type. The serological results agree with the occupation of the patients, nearly all the K type cases being among coolies on estates, the W type including clerks, shop keepers, engine drivers, etc., mostly urban dwellers. *D. H.*

VITALIS (F.). Een geval van tropical typhus te Koedoes. [**A Case of Tropical Typhus at Koedoes, Java.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Jan. 2. Vol. 74. No. 1. pp. 52–56.

A record is given here of the occurrence of a case of "shop-typhus" with a full account of the clinical history. As is common in these cases the diagnosis was not made immediately and those of dengue and typhoid were first considered. The proof that the case was one of typhus was given by the positive serum agglutination reaction with Proteus OX19 at 1/800. This reaction was negative for the Kingsbury strain. *W. F. Harvey.*

BRIDGES (R. F.). **Tropical Typhus and the Weil-Felix Reaction.**—*Jl. Roy. Army Med. Corps.* 1934. Feb. Vol. 62. No. 2. pp. 102–106.

Such a paper as this, which gives full and detailed instruction regarding the principles and the methods of carrying out the Weil-Felix reaction, was wanted not only in India and is well done.

There has often been little uniformity in carrying out the test, one reason being that Proteus cultures of pure O type were often not obtainable and when available were not reliable. It is now proposed to issue stock emulsions of 3 strains of Proteus, X19, X2 and XK, from the laboratory at Kasauli. The author also urges anyone who may have a case of tropical typhus under his care to make every effort to isolate a strain of Proteus from the blood or urine and to test such a strain against the serum of the patient and against specific sera which are to be supplied from the Central Laboratory along with the cultures.

If the instructions in the paper are carefully followed it may be found that there are 3 types of typhus in India:—1. Epidemic typhus (louse borne). 2. Endemic typhus (flea borne). 3. Tick typhus (tick borne); the last variety being closely related to the Eastern type of Rocky Mountain fever and to boutonneuse fever of Southern Europe and North Africa.

[It is not generally known that boutonneuse fever has already been described as such in India; see this *Bulletin*, LINDBERG, Vol. 29, pp. 19 & 458.] *D. H.*

VIEIRA (Francisco Borges) & MESQUITA (Mario). Alguns aspectos epidemiologicos do "tifo exantematico de S. Paulo." [**Some Epidemiological Aspects of São Paulo Typhus.**]—Reprinted from *Rev. Hyg. e Saude Publica.* 1934. Jan. pp. 1–25. With 4 figs. & 1 map. [15 refs.] [Issued as Boletim No. 51 do Inst. de Higiene, São Paulo.]

The incidence and case fatality of typhus at São Paulo from October 1929 to October 1933 was as follows :—

	Cases	Deaths	Fatality
			Per cent.
1929	15	14	93·3
1930	21	14	66·6
1931	28	19	67·8
1932	15	11	73·3
1933	9	8	88·8
	88	66	75·0

Each year the highest incidence was in November (25 of the 88 cases). Lice or any other ectoparasites were exceptional. Only 10 per cent. showed head or body lice and 43 per cent. showed none, while no information was forthcoming in 53 per cent. 50 patients were males and 38 females. The ages ranged from 2 to 74, but the highest proportion (12 cases) were found in the age period 10–14. The cases were mainly confined to certain parts of the city, preferably the suburban areas. Most of the cases occurred in houses bordering on untilled soil or woodland. In contrast with the sporadic character of endemic typhus this concentrates in certain zones, as is frequently observed in Rocky Mountain spotted fever of which São Paulo typhus is probably a variety. *J. D. Rolleston.*

MONTEIRO (J. Lemos). Etude comparative du "typhus exanthématique de Sao Paulo" (rickettsiose néotropique) et du "typhus exanthématique" d'autres lieux, basée sur l'epreuve de protection par le sérum de convalescent. [**Comparative Study of Sao Paulo Typhus and True Typhus based on Protection Tests with the Serum of Convalescents.**]—*C. R. Soc. Biol.* 1934. Vol. 115. No. 12. pp. 1360–1362.

The serum was obtained from a case of true typhus in the Argentina and was mixed with Sao Paulo virus (blood of guineapigs taken at height of fever) 0·5 cc. of serum and 0·1 cc., 0·25 and 0·4 cc. of guineapig blood containing virus. No. 1 serum only protected against the minimal dose of virus. Control guineapigs, virus only, all died. Similar tests using the virus of Rocky Mountain fever gave a like negative result. *D. H.*

DAVIS (Gordon E.) & PARKER (R. R.). **Comparative Experiments on Spotted Fever and Boutonneuse Fever.**—*Public Health Rep.* 1934. Mar. 30. Vol. 49. No. 13. pp. 423–428. With 2 charts.

The authors and others have already shown that there is definite cross immunity between the viruses of Rocky Mountain fever and of

boutonneuse fever and between Rocky Mountain fever and Sao Paulo fever; but although Rocky Mountain fever vaccine protects guineapigs against Sao Paulo fever, the work presented in the present paper shows that Rocky Mountain fever vaccine does *not* protect against the virus of boutonneuse fever. *D. H.*

JELLISON (William L.). **Rocky Mountain Spotted Fever. The Susceptibility of Mice.**—*Public Health Rep.* 1934. Mar. 16. Vol. 49. No. 11. pp. 363–367.

The opinion is generally held that small mammalian hosts of ticks act as reservoirs of infection for Rocky Mountain fever. Previously it was thought that mice were not susceptible to the virus. But this paper clearly shows that the "meadow" mouse is extremely susceptible to the virus and the "deer" mouse slightly susceptible; as the meadow mouse is an important host of the tick *D. variabilis* it is possible that this small mammal may play a considerable part in the natural maintenance and spread of the disease. House mice were distinctly resistant to the virus. *D. H.*

DAVIS (Gordon E.), PARKER (R. R.) & WALKER (Mary E.). **Further Observations on the Agglutination of Proteus X Strains in Rocky Mountain Spotted Fever (II).**—*Public Health Rep.* 1934. Mar. 2. Vol. 49. No. 9. pp. 298–311.

The sera of 81 cases of fever were tested in this investigation and 13 strains of Proteus X were used. All but 3 of X19 strains were H variants. In 57 cases only single samples were tested. The results are fully set out in tables. The results of H type agglutinations are not recorded.

OX19 (504) a pure O antigen gave the following results: Of 27 samples taken during the first 9 days of illness 37 per cent. gave a positive reaction of 1/160 or higher. Of 31 samples taken from the 10th to the 15th day 83 per cent. showed significant agglutination all above 1/160 and as high as 1/5120. Of 26 samples taken from the 16th to the 26th day 80 per cent. showed a significant titre.

The use of the strain OXK gave the following results: out of the 100 samples of sera tested at various periods during illness and convalescence only one gave a definite positive reaction up to a dilution of 1/320.

It is recommended that in carrying out agglutination tests on Rocky Mountain fever cases 3 samples of serum should be taken, one as early as possible in the disease, the second during the period from the 10th day of illness to cessation of fever, and the 3rd about the end of the first week of convalescence. The authors prefer to use emulsions of living bacilli and the tests should be left 48 hours before reading results. *D. H.*

BREINL (F.). Versuche zur Züchtung des Felsenfiebervirus in vitro. [**Cultivation of the Virus of Rocky Mountain Fever in Vitro.**]—*Zent. f. Bakt.* I. Abt. Orig. 1933. Dec. 29. Vol. 130. No. 5/6. p. 316–319.

The medium employed consisted of cells of chick embryo emulsified and mixed with virus obtained from the testicle of guineapigs with

high fever, inoculated into 3 cc. of tyrode solution + 1 cc. normal rabbit serum.

After 7 days incubation at 35°C. 1 cc. of the fluid with some tissue cells was removed ; one part of this was utilized to make subcultures and one part injected into guineapigs. The results are shown in graphic form.

In 1/3 of the cases successful culture resulted and in one series the culture was kept alive through 7 subcultures ; in each case the virus was shown to be infective for guineapigs. In none of the cultures were Rickèttsia observed. *D. H.*

ANDRÉOLI & CHARLET. Fièvre boutonneuse et troubles oculaires. [**Boutonneuse Fever and Eye Symptoms.**]—*Bull. Acad. Méd.* 1934. Mar. 6. 98th Year. 3rd Ser. Vol. 111. No. 9. pp. 338–347.

A number of cases of boutonneuse fever have been reported in which the site of inoculation of the virus is the conjunctiva ; they are usually due to rubbing the eye with a finger contaminated by crushed dog ticks. 20 such cases are analysed by the authors, who regard them mainly from the oculist's point of view.

The average incubation period was 3 days ; the rash appears on or about the 5th day after the commencement of the conjunctivitis, which may last for 8 days but a redness may be noted up to one month ; there is oedema of the eyelid with suppuration in the culs-de-sac and inflammation of the lymphatics leading to the preauricular lymphatic glands. The conjunctivitis is as a rule one-sided. The disease following is generally but not always of a severe type especially as regards the nervous symptoms.

The oculist is called in to see the patient at first and the physician later when the fever and rash appear ; oculists therefore should be on the outlook for such cases especially in endemic areas. *D. H.*

PREVITERA (Antonino). Ricerche sperimentali in alcuni casi di tifo esantematico benigno endemico in Catania. [**Experimental Researches in Cases of Mild Endemic Typhus.**]—*Ann. d'Igiene.* 1934. Mar. Vol. 44. No. 3. pp. 212–224. With 2 charts. [11 refs.]

A record of two cases in adults of mild endemic typhus corresponding to the summer typhus described by OLMER and others as occurring in the Marseilles district and on the Mediterranean coast. Their blood was inoculated into guineapigs with the following results : (1) All showed a rise of temperature and three out of six had a scrotal reaction visible to the naked eye during life in one animal, and on histological examination post mortem in the other two. (2) The virus was transmissible in series up to the fourth passage without becoming attenuated. (3) Inoculation did not produce any immunity, as two animals showed a marked rise of temperature when injected, again, the one 45 days and the other 32 days after the first inoculation. (4) The Weil-Felix reaction was constantly negative and Rickettsia could not be found in the inoculated animals. *J. D. Rolleston.*

LEMIERRE (A.). **Eruptive Mediterranean Fever.**—*Lancet.* 1934. Mar. 3. pp. 441–443. [24 refs.]

An address delivered at the Middlesex Medical Society, January 23rd.

Professor Lemierre describes a case of "Eruptive Mediterranean Fever" which came under his observation in the American Hospital in Paris; this man had been infected by the bite of dog ticks while in Italy and developed the disease 12 days later on his arrival in Paris. The remainder of the address consists of an able review of recent work on this disease carried out in France, Italy and elsewhere; all the articles referred to have been already summarized in this *Bulletin*.

[It is rather disappointing (especially to the reviewer) that Professor Lemierre has no better English name for this disease than "Eruptive Mediterranean Fever"; in one place also he refers to the disease as "Mediterranean" fever, which must be confusing to English readers as this is or was a common name for "Malta fever."] *D. H.*

MONTEIRO (J. Lemos). A propos de la *Rickettsia mooseri*. [*R. mooseri*.]—*C. R. Soc. Biol.* 1934. Vol. 115. No. 12. pp. 1358–1359.

WEIGL and NICOLLE recently proposed the name *Rickettsia mooseri* for the organisms found in animals and insects infected with the virus of Mexican typhus fever (*ante*, p. 244); Monteiro points out that he had suggested this name in a paper published some months earlier. *D. H.*

LEMIERRE (A.). Sur un cas de fièvre boutonneuse méditerranéenne observé à Paris.—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1934. Feb. 5. 50th Year. 3rd Ser. No. 3. pp. 106–109.

LEMOINE & LE MER. Sur un cas de fièvre boutonneuse.—*Tunisie Méd.* 1934. Feb. Vol. 28. No. 2. pp. 43–47.

PLAZY, MARCANDIER & PIROT. Fièvre boutonneuse dans le milieu maritime à Toulon.—*Arch. Méd. et Pharm. Nav.* 1934. Jan.–Feb.–Mar. Vol. 124. No. 1. pp. 80–92. [16 refs.]

SCADUTO (Pasquale). Un caso di febbre esantematica mediterranea nei dintorni di Tripoli.—*Arch. Ital. Sci. Med. Colon.* 1934. Mar. 1. Vol. 15. No. 3. pp. 173–179. English summary (3 lines).

SCATURRO (Alberto). La febbre bottonosa. Rivista sintetica e casi personali.—*Riv. Sanitaria Siciliana.* 1934. Mar. 15. Vol. 22. No. 6. pp. 433–436, 439–442. English summary (3 lines).

RABIES.

A REVIEW OF RECENT ARTICLES. XXI.*

i. *Virus.*

By a very ingenious method of technique it would appear that NICOLAU and KOPCIOWSKA[1] have succeeded in retransforming fixed virus into street virus. The strain of fixed virus used had been passaged in the laboratory for 6 years, and gave rise to from 1 to 4 Negri bodies in 100 ganglion cells of the horn of Ammon. The transformation was achieved by passage inoculations made into the *right* sciatic nerve, the emulsions employed being obtained from the *left* sciatic nerve of the previous animal. A control animal was inoculated intracerebrally at each subpassage. With a great deal of trouble two lines of passage have been obtained covering a period of more than a year. "If one judges by the number and size of the Negri bodies, which from the 4th or 5th passage from nerve to nerve are found on the hippocampi of the control animals, then we may be permitted to affirm, from this moment, that the transformation of fixed into street virus is possible." The numbers of Negri bodies in the control animals inoculated from the 2nd, 3rd, 4th, and 7th passages were 11, 62, 17 and 102 per 100 neurones in one series, and 28, 21, 160 and 92 in the other. In addition, in the spinal ganglia of the animals of the 3rd, 5th and 6th passages the numbers in one series were 209, 208, and 168 per 100 neurones, and in the 3rd and 4th passages of the other series 300 and 152.

The rôle of the vampire bat in the transmission of rabies both of man and of cattle has been referred to on various occasions in previous reviews (Vol. 29, pp. 595 and 596). LIMA[2] presents further evidence in support of the view that this animal, *Desmodus rotundus*, is the transmitter of the epizootics in the Matto Grosso region of Brazil. He refers to experiments which show that vampire bats fed on infected cattle do not become infected. Of a number of uninfected bats kept in the same cage as a number of infected bats, one developed the disease, and in a third experiment four infected bats remained in health though at the same time they transmitted infection to 25 cattle. One of the bats was killed and its salivary gland was found to be infective to guineapigs. A vampire bat may therefore harbour infection, and be capable of transmitting it, without showing any symptoms of rabies. It is well known that those regions of the State of Santa Catherina in which epizootics are prevalent are also the favourite haunts of the Desmodontidae. The author concludes from his observations and experiments that it may be taken as "decisively and completely proved" that in the epizootics of rabies in Santa Catharina the transmitter is the vampire bat (*Desmodus rotundus*).

---

*For the twentieth of this series see Vol. 31, p. 145.

[1] NICOLAU (S.) & KOPCIOWSKA (L.). Sur la transformation du virus rabique fixe en virus des rues.—*C. R. Acad. Sci.* 1934. Feb. 5. Vol. 198. No. 6. pp. 622–624.

[2] LIMA (Esperidião de Queiroz). A transmissão da raiva bovina pelo morcego hematophago *Desmodus rotundus*.—*Brasil-Medico.* 1934. Jan. 20. Vol. 48. No. 3. pp. 38–40.

LEVADITI, SCHOEN, and LEVADITI[3] have carried out experiments designed to determine what is the ultimate fate of Negri bodies introduced into the receptive tissues of a fresh animal. Thus a thick emulsion of brain, rich in Negri bodies, was injected into the anterior chamber of the eye. The animals injected were examined from 24 hours up to the time of death, and the tissues at the site of inoculation have been examined histologically. It appeared that the inoculated neurones degenerated, and that at no time could one detect the presence of Negri bodies.

"The evolution of the Negri bodies ceases at the moment of injection, which appears to show that their life is ephemeral and intimately associated with that of the neurones which harbour them. The most plausible hypothesis is that the Negri bodies resolve themselves into infra-visible elements which invade the nervous system and multiply in it. After penetrating certain neurones they develop into the visible phase of the cycle of evolution, the Negri body."

The effect of pH on the virulence of fixed virus has been studied by KOLDAJEW and PIKUL[4]. The investigation was carried out on 649 rabbits, of which 308 developed the disease. The result is shown by a graph, from which it appears that the optimum pH lies between 6·4 and 7·0. By changing the pH the persistence of virulence is reduced, falling more quickly as acidity increases, and more slowly as alkalinity increases. This loss of virulence is probably an irreversible phenomenon.

SHORTT and BROOKS[5] have extended CLIFTON's work on the photodynamic action of methylene blue on Bacteriophage, to the virus of rabies. The dilutions of the dye which were employed were 1 in 10, 20 and 200 thousand. These were added to the supernatants of suspensions of fixed virus brain tissue, centrifuged until they were opalescent. Certain mixtures were exposed to daylight for from 2 to 60 minutes, others were kept in the dark room.

It was found that after 10 minutes exposure all three dilutions of methylene blue completely inactivated the virus; and that the lowest dilution of the stain was less effective than the two higher dilutions. This latter result is in agreement with "the experiments of PERDRAU and TODD, which showed the inactivating effect of a screen of methylene blue" upon the penetration of the light. The protective action of homologous living cells which has been described in the case of the viruses of herpes, Borna disease, and fowl plague was not observed, "and this fact brings rabies fixed virus into line, so far as this character is concerned, with the viruses of louping ill and vaccinia."

A communication of a very similar nature is made by GALLOWAY[6]. He has shown that the photodynamic action of methylene blue

---

[3] LEVADITI (C.), SCHOEN (R.) & LEVADITI (Jean). Cycle évolutif du virus rabique.—*C. R. Soc. Biol.* 1934. Vol. 115. No. 13. pp. 1502–1504.

[4] KOLDAJEW (B.) & PIKUL (N.). Ueber den Einfluss der H-Ionenkonzentration auf das Virus fixe der Tollwut.—*Zent. f. Bakt.* I. Abt. Orig. 1934. Feb. 28. Vol. 131. No. 1/2. pp. 6–9. With 1 fig.

[5] SHORTT (H. E.) & BROOKS (A. G.). Photodynamic Action of Methylene Blue on Fixed Rabies Virus.—*Indian Jl. Med. Res.* 1934. Jan. Vol. 21. No. 3. pp. 581–585.

[6] GALLOWAY (I. A.). The "Fixed" Virus of Rabies: the Antigenic Value of the Virus Inactivated by the Photodynamic Action of Methylene-Blue and Proflavine.—*Brit. Jl. Experim. Path.* 1934. Apr. Vol. 15. No. 2. pp. 97–105.

inactivates fixed rabies virus in collodion membrane or sand and paper pulp filtrates, but not in unfiltered suspensions. The virus appears to be relatively more sensitive to the photodynamic action of proflavine than to that of methylene blue. It is shown that when inactivated the virus retains its antigenic potency since 26 out of 31 rabbits (84 per cent.) which had received more than one dose of such a vaccine survived an intramuscular test dose of fresh virus, while of 16 unvaccinated control animals only 1 survived (6 per cent.).

Much has been written of late years on the pseudorabies of AUJESKY. REMLINGER and BAILLY[7] now contribute an admirable summary based to a large extent upon original experiments. They have investigated the disease in rabbit, cat, dog, jackal, hedgehog, mouse, guineapig, pig, hen, goose, duck, pigeon, buzzard and hawk. The modes of infection have been examined in detail. They show that transmission may occur by inoculation on the mucous membranes, inoculation on or into the skin, or by ingestion. The disease is described in detail and in a tabular summary its main features are contrasted with those of true rabies.

TRAUB[8] has succeeded in cultivating the virus of pseudorabies in the presence of living tissue. The fact that the virus failed to multiply in tissue which had been stored in the refrigerator for more than 6 days prior to inoculation with the virus, and in cell-free 20 per cent. rabbit testicle extract, suggests that living cells are necessary for its growth. Growth has been obtained in media containing rabbit or guineapig testicle or chick embryo tissues. Rabbit testicle tissue gave the best results both as to regularity of the multiplication of the virus and the concentration the virus attained in cultures. The chick embryo medium, however, is the simplest, as it does not require serum, while the testicle media must contain a certain amount of homologous serum to ensure multiplication of the virus. In rabbit kidney tissue pseudo-rabies virus could not be grown.

The testicular medium is prepared as follows. 100 to 150 mgm. of testes washed in saline and minced, is placed in 50 cc. flasks. Two cc. of serum and 2 cc. of Tyrode solution prepared according to the formula of Fischer are added. The flask is shaken, and plugged with cotton wool covered by a layer of tinfoil. To prepare the chick embryo medium, 10-day embryos are cut up and mixed with scissors, after the eyes have been removed, and 100–150 mgm. of pulp is suspended in 3 cc. Tyrode solution to 1 cc. sheep serum. (It appeared in later experiments that the presence of sheep serum was not necessary).

The pathogenic properties of the virus were not altered during 49 serial cultural passages, and there were merely quantitative differences between the cultivated virus and rabbit brain passage virus.

It is stated that in sections of rabbit testicular cultures incubated for 1 day no inclusion bodies were apparent, whereas after 2 and 3 days they were seen in the interstitial cells of Leydig, in endothelial cells

---

[7] REMLINGER (P.) & BAILLY (J.). Contribution à l'étude du virus de la "maladie d'Aujeszky."—*Ann. Inst. Pasteur.* 1934. Apr. Vol. 52. No. 4. pp. 361–405.

[8] TRAUB (Erich). Cultivation of Pseudorabies Virus.—*Jl. Experim. Med.* 1933. Dec. 1. Vol. 58. No. 6. pp. 663–681. With 3 figs. on 1 plate. [21 refs.]

of capillaries, and in connective tissue cells of the lamellar membranes of the tubules but not in the seminiferous epithelial cells. After four days these were no longer distinct.

ii. *Symptomatology and Diagnosis.*

A case of hydrophobia presenting no unusual features is described by GUPTA.[9]

ZOTTNER[10] recommends the following as a simple and rapid method for staining Negri bodies :—

(1) Paraffin removed by xylol : wash in absolute alcohol.
(2) Without washing, cover the section with a few drops of nitric acid (1/3) : leave for 2 or 3 minutes, pour off the acid solution.
(3) Without washing pour on a few drops of Ziehl's fuchsine, 15 seconds.
(4) Wash quickly, and apply for 15 seconds a freshly prepared mixture of equal parts of saturated picric acid (aqueous solution) and 1 per cent. indigo carmine.
(5) Dehydrate and differentiate in absolute alcohol. When the sections commence to take on a green tint, clear with xylol and mount.

The Negri bodies are stained red, the neuroglia green, protoplasm green or green violet, nucleoli and chromatin granules dark brown.

iii. *Pathology.*

From a series of 6 experiments on 19 animals REMLINGER and BAILLY[11] find that the rabies virus can be detected in the lung "rarely but not exceptionally" (6 times in 19, *i.e.*, 32 per cent.). This proportion is similar to that formed for the spleen (28 per cent.), the liver (30 per cent.) and the kidney (30 per cent.).

The view that rabies antibodies are formed in the brain, led to the attempt to immunize by intracerebral inoculation. It was found by REMLINGER and BAILLY (this *Bulletin*, Vol. 26, p. 222) and by LÖFFLER and SCHWEINBURG (*loc. cit.*, Vol. 28, p. 745) that such a method of treatment gave rise to no immunity. The latter authors then presented evidence that the site of antibody formation was the reticulo-endothelial system (this *Bulletin*, Vol. 30, p. 138), and that blocking of this system reduced protection. They now[12] present further evidence in favour of the reticulo-endothelial theory, and show that a previously established immunity can be rendered ineffective by blocking. The rabicidal antibodies are however not reduced by blocking. The experiments were carried out on 26 rabbits ; the results are clear cut, and in each case the observation was controlled.

It will be remembered that MARIE in his later experiments (see this *Bulletin*, Vol. 30, p. 579) found that though even large doses of fixed virus did not infect the guineapig when introduced intraperitoneally, previous injection with Indian ink emulsion rendered

---

[9] GUPTA (Rabindar Chandra Das). A Case of Hydrophobia after Preventive Inoculation.—*Indian Med. Gaz.* 1934. Feb. Vol. 69. No. 2. p. 81.

[10] ZOTTNER (G.). Coloration simple, sûre et rapide des corpuscules de Negri dans les coupes.—*C. R. Soc. Biol.* 1934. Vol. 115. No. 6. pp. 593–594.

[11] REMLINGER (P.) & BAILLY (J.). Sur la présence du virus rabique dans le poumon.—*Bull. Acad. Méd.* 1934. Jan. 30. 98th Year. 3rd Ser. Vol. 111. No. 4. pp. 159–164.

[12] LÖFFLER (Ernst) & SCHWEINBURG (Fritz). Beitrag zur Theorie der Immunität bei Tollwut.—*Zent. f. Bakt.* I. Abt. Orig. 1933. Dec. 29. Vol. 130. No. 5/6. pp. 329–334. [10 refs.]

them susceptible. Further observations on this subject are submitted by PATTO and CARNEIRO[13]. From experiments carried out with the viruses of rabies, and of Aujesky's pseudo-rabies, they conclude that subcutaneous, intravenous, and even intraspinal injections of the blockading dyestuff causes the immunity of vaccinated animals to disappear, and further that the virulence of pseudo-rabies is greatly enhanced by simultaneous injections of Nankin ink. It was also found that the complement content of the serum of blocked animals fell slightly after an interval of 2 hours, and returned to normal after 24 hours. The authors then go on to describe their experiences with crossed precipitation tests, with which they obtained results specific for the two viruses.

A similar result has been attained by MARIE[14]. Using Indian ink, all of 12 blocked guineapigs died of rabies, whereas of 12 unblocked only 2 developed the disease, and using Van Deinse's mixture, 3 of 6 blocked, and none of 6 unblocked succumbed.

That Negri bodies may be found in the sympathetic nerve ganglia scattered throughout the salivary glands was pointed out by MANOUÉLIAN and VIALA (this *Bulletin*, Vol. 25, p. 707). Other conformations not confined to ganglion cells have from time to time been described by these and other authors. SHORTT and LAHIRI[15] have made an extensive study of salivary glands from dogs, monkeys, and man, and whilst they confirm the existence of Negri bodies within ganglion cells, they come to a different conclusion regarding many of the other structures which have been described.

Many curious appearances were seen in the acinar cells, some granular, some like Negri bodies with inner formations, but these, in the view of the authors, are characteristic of hyperstimulation of the gland, and are not directly indicative of the presence of a living virus, although the latter is probably the cause of the stimulation in rabies. For example, bodies which stained red with Mann's stain are considered to be of the nature of coagulated secretion or its precursors, and these have actually been produced experimentally by the exhibition of pilocarpine. The final conclusion of the authors is that (apart of course from inclusion bodies in nerve cells) " no evidence was obtained of the visible presence of any bodies which could be identified as bacteria, protozoa, or filterable viruses, or indeed of any living causative agent."

The paper should be studied in detail by those who are interested in the histology of rabies.

Observations on the rate of dissemination of rabies virus introduced into a sciatic nerve are described by NICOLAU and KOPCIOWSKA.[16]

---

[13] PATTO (Ortiz) & CARNEIRO (J. M.). Questões de immunidade na raiva e na pseudo-raiva.—*Brasil-Medico.* 1933. July 8. Vol. 47. No. 27. pp. 474–480. [46 refs.] English summary.

[14] MARIE (A. C.). De l'infection rabique par la voie péritonéale.—*Ann. Inst. Pasteur.* 1934. Feb. Vol. 52. No. 2. pp. 141–145. [11 refs.]

[15] SHORTT (H. E.) & LAHIRI (B. N.). Morphological Studies on Rabies. Part I. The Salivary Glands.—*Indian Jl. Med. Res.* 1934. Jan. Vol. 21. No. 3. pp. 587–604. With 23 coloured figs. on 2 plates.

[16] NICOLAU (S.) & KOPCIOWSKA (L.). Etude de la dispersion, dans le système nerveux du lapin, du virus rabique des rues inoculé dans un nerf périphérique.—*C. R. Soc. Biol.* 1934. Vol. 115. No. 3. pp. 262–264. With 1 fig.

It appears from these that the virus arrives simultaneously in the medulla and in the opposite sciatic nerve about the 7th day after inoculation.

iv. *Methods of Treatment and Statistics.*

Successful results have been obtained by PROCA, BOBES, and JONNESCO[17] in the preventive serotherapy of rabies. The results of their experiments are as follows :—

	Treated			Controls		
	Survived	Died	Total	Survived	Died	Total
Series A ...	2	0	2	0	2	2
B ...	3	1	4	2	2	4
C ...	2	2	4	1	3	4
D ...	4	1	5	2	3	5
	11	4	15	5	10	15

In series A and B the infecting dose was 0·2 cc. of a 1/10 emulsion of fixed virus injected into the sole of the foot. 3 cc. of sheep antirabic serum (with a neutralizing titre of 1 to 1) was immediately thereafter injected into the flank of the same side.

In series C the dose of serum was given 24 hours before the infecting dose, whilst in series D, 5 cc. of serum were inoculated immediately after the infecting dose, a similar dose being administered 24 hours later, and doses of 2 cc. were given intramuscularly for a further period of a week. It would thus appear that the antirabic serum had a definite preventive action.

In a second communication[18] they describe experiments on rabbits and mice in which the infecting dose was introduced into the tail. It appeared that under these conditions antirabic serum was ineffective, probably, in their opinion, on account of the richness of the tail in nerve endings.

It will be remembered (this *Bulletin,* Vol. 30, p. 581) that CUNNINGHAM, MALONE and GRAIGHEAD from experiments on monkeys showed that the "Paris" strain of fixed virus conferred a more solid immunity than the "Kasauli" strain (isolated from a dog at Kasauli, and in general use in India). SHORTT, MALONE, CRAIGHEAD, and MCGUIRE,[19] now record the results of a large experiment on alternate human cases, contrasting the antigenic values of the two strains. 6,173 persons were treated by the Kasauli strain, and 6,150 by the Paris strain. The authors consider that Class IV cases (*i.e.* (*a*) deep extensive bites on all parts of the body, or (*b*) all bites

[17] PROCA (G.), BOBES (S.) & JONNESCO (D.). Sur la sérothérapie préventive de la rage.—*C. R. Soc. Biol.* 1934. Vol. 115. No. 9. pp. 1001–1003.

[18] PROCA (G.), BOBES (S.) & JONNESCO (D.). Inoculation intracaudale du virus rabique et sérothérapie de la rage.—*C. R. Soc. Biol.* 1934. Vol. 115. No. 12. pp. 1313–1315.

[19] SHORTT (H. E.), MALONE (R. H.), CRAIGHEAD (A. C.) & MCGUIRE (J. P.). An Investigation into the Relative Immunizing Value of the Kasauli and Paris Strains of Rabies Fixed Virus.—*Indian Med. Res. Memoirs. Supplementary Series to Indian Jl. Med. Res.* 1934. Jan. Memoir No. 28. 78 pp.

and scratches on the head and neck), bring out the contrast most clearly. These may be subdivided according to position of bite as follows :—

	Carbolized 5 per cent. Paris sheep vaccine			Carbolized 5 per cent. Kasauli sheep vaccine		
	Cases	Deaths	Mortality	Cases	Deaths	Mortality
Leg	556	13	2·34	584	12	2·05
Trunk ...	11	2	18·18	16	0	—
Arm... ...	267	8	3·00	279	10	3·58
Multiple ...	171	6	3·51	171	14	8·19
Face ...	227	20	8·81	191	16	8·38
Multiple face	196	4	2·04	180	20	11·11
Total ...	1,428	53	3·71	1,421	72	5·07

It should be explained that "Multiple Face" denotes persons bitten on more than one of the primary positions one of which is the head, whereas "Multiple" denotes those bitten in more than one position excluding the head. [The difference in the total figures is insignificant, $P = 0{\cdot}1$, and the only figures which show statistically significant differences are those of the multiple face group. It is difficult to understand why this particular group should be the only one which exhibits a significant difference. Further examination of the figures shows that the number of bites is not the deciding factor. Thus it would appear that the difference, if it be a real one, must depend essentially on multiplicity of position. This conclusion, however, is one which it is difficult to accept. For these and other reasons the claim of the authors that the human inoculation experiments demonstrate that the Paris strain is superior in immunizing properties to the Kasauli strain cannot be considered to be completely proved. However, it is in conformity with the results previously arrived at by CUNNINGHAM, and the general effect of the cumulative evidence is in favour of the conclusion being correct.]

An attempt was also made by experiments on monkeys with the same object. The final figures in an experiment in which the infecting dose was given after immunization are as follows :—

Strain	Died	Survived	Total	Mortality
Kasauli	21	75	96	21·9
Paris	16	75	91	15·7
Controls	36	15	51	70·6

[From these figures it appears that immunization by either strain is better than nothing, but that no significant difference can be detected between the two strains. The probable order of efficiency of the three groups is, as in the experiments of CUNNINGHAM and his co-workers, Paris, Kasauli, Controls, but the experiment has again failed to establish the existence of a clear statistical difference between the results obtained with the two viruses. A further experiment in which

the infecting dose was given before immunization leads to the same order of efficiency though statistical methods again fail to demonstrate significant differences between the immunizing properties of the two strains.] The result of this experiment may be summarized as follows :—

Strain	Died	Survived	Total	Mortality
Kasauli	59	29	88	67·1
Paris	56	34	90	62·2
Controls	33	8	41	80·5

[The difference between Paris virus and the controls is significant, but that between Kasauli virus and controls is not. Although each of these sets of observations seems to be inconclusive with regard to the difference between the two strains when taken separately, yet the weight of the evidence appears to be in favour of the view that the Paris strain is somewhat better than the Kasauli strain as an immunizing agent.] The authors finally stress the point that the actual numbers of deaths during successive years, " are considered a much better indication of improving results than the percentage death rate. The latter may easily be artificially lowered by the inclusion in statistics of large numbers of patients not really at risk, whereas the total deaths cannot be obscured in any way." The following table is appended.

Year	Total treated	Total deaths	Percentage death rate
1925	8,632	138	1·60
1926	8,372	149	1·78
1927	8,437	126	1·49
1928	8,574	103	1·20
1929	8,365	135	1·61
1930	9,653	118	1·22
1931	11,147	107	0·96
1932	12,801	73	0·57

"A perusal of the table will make evident the great improvement in the year 1932, corresponding with the introduction of the new line of treatment" (Paris strain of fixed virus). " This fall corresponded so exactly with the introduction of the exclusive use of Paris virus, combined with a dosage which entailed a higher average dose of brain substance per patient, that it seems fair to draw the conclusion that these factors were causally connected." [Although this evidence must be taken into account, it is essentially uncontrolled, and there are many conceivable factors which might bring about a reduction in the total deaths from rabies amongst those treated at the Institute. It has not the statistical value of the alternative case observations or of the animal experiments mentioned above.]

A fourth review, by McKendrick,[20] of statistics from Pasteur Institutes on the results of antirabic treatment, undertaken by the

[20] McKendrick (A. G.). A Fourth Analytical Review of Report from Pasteur Institutes on the Results of Anti-Rabies Treatment.—*Quart. Bull. Health Organisation League of Nations.* Geneva. 1933. Dec. Vol. 2. No. 4. pp. 553–599.

Health Section of the League of Nations at the instance of the International Rabies Conference (Paris 1934) has appeared. It deals with data relating to 119,433 persons treated, and relates mainly to the year 1931. The author in drawing his conclusions has in certain cases made use of the combined statistics of all four reviews.

It was pointed out in previous reviews that the state of risk of the treated non-European was much higher than that of the treated European. From the massed figures it appears that the mortalities are in the ratio of 6·5 to 1.

No evidence has been formed indicating that any one of the methods of treatment followed is superior as an immunizing agent to any other. For example the massed figures for Europeans bitten by dogs which were certified as rabid (Categories A and B) are as follows :—

	Number treated	Deaths		Mortality
		Observed	Calculated	
Europeans.				
1. Cords	3,997	10	7·6	0·25
2. Dilutions ...	6,362	11	12·1	0·17
3. Killed phenol ...	5,554	6	10·5	0·11
4. Live phenol ...	738	2	1·4	0·27
5. Fermi original ...	3	0	0·01	0·0
6. Fermi sero-vaccine	28	0	0·05	0·0
7. Heated	7,377	17	14·0	0·23
8. Ether killed ...	7,034	12	13·3	0·17
9. Mixed	15,774	27	30·0	0·17
10. Yatren	2,271	8	4·3	0·35
11. Boecker	931	2	1·8	0·22
	50,069	95	95·0	0·19

Comparison of the observed rabies with those calculated from the average mortality shows that the differences are only slight—in fact such divergences would be expected to occur in samples of a homogeneous population two times out of five.

A similar result appears in the non-European figures.

The facts regarding lateness of arrival put forth in the following table are interesting :—

	Number treated	Deaths		Mortality
		Observed	Calculated	
Europeans.				
0–4 days late ...	90,813	129	117	0·14
5–7 ,, ...	28,378	32	37	0·11
8–14 ,, ...	17,366	16	22	0·09
more than 14 days late	7,256	9	9	0·12
	143,813	186	185	0·13

	Number treated	Deaths		Mortality
		Observed	Calculated	
Non-Europeans.				
0–4 days late ...	25,528	212	210	0·83
5–7 ,, ...	8,652	57	71	0·66
8–14 ,, ...	5,734	41	47	0·72
more than 14 days late	2,960	43	24	1·45
	42,874	353	352	0·82

Thus in the case of Europeans no evidence of an increase in mortality with lateness of arrival can be detected. On the other hand in the case of non-Europeans there is a significant rise between the 3rd and 4th periods (P = 0·0009). The tendency for mortalities to vary with lateness of arrival is a complex phenomenon depending upon a number of factors, and an increase cannot be taken as a simple and direct indication of the value of treatment. The question is discussed in some detail in the review.

From figures relating to 290,337 persons it appears that the liability to post-vaccinial paralysis amongst those treated by "live" vaccines is 4·4 times as great as amongst those treated by "killed" vaccines, and 11 times as great as amongst those treated by "heated" vaccines.

A report on antirabies treatment in the U.S.S.R. follows. This deals with figures relating to the years 1927, 1928, 1929 and 1930, the numbers of persons treated being 74,430, 66,154, 53,518, and 49,399—a total of 243,501. The mortalities during the four years were respectively 0·23, 0·20, 0·15, and 0·11 per cent. In fact the reduction in the number treated has been accompanied by a decline in mortality. These two phenomena are difficult to interpret and an exhaustive statistical analysis has been made of the various factors regarding which data were available. The reduction in the number presenting themselves for treatment, and in particular of those bitten by wolves, might be accounted for by assuming that a reduction had occurred in the chance of being bitten, *e.g.*, by a reduction in the number of rabid animals, or by a redistribution of the human population of those parts of Russia from which the patients were drawn. The reduction in mortality is partly accounted for by a reduction in the proportion of those bitten by wolves, and also by the fact that delay in coming for treatment had been reduced. No other significant changes in the type of case coming for treatment appear to have occurred. In the presence of these profound changes, which appear to be largely if not wholly sociological in origin, it has not been found possible to arrive at any conclusion regarding the efficacies of the various methods of treatment employed.

A summary of the results of antirabic treatment at Tonking (Indo-China) is given by GENEVRAY and DODERO.[21] The method of treatment is that of Calmette, and the course lasts from 15 to 20 days.

[21] GENEVRAY (J.) & DODERO (J.). Traitement antirabique au Tonkin et mortalité chez les sujets traités pendant une période de sept années (1er janvier 1926—31 décembre 1932).—*Ann. Inst. Pasteur.* 1934. Mar. Vol. 52. No. 3. pp. 352–360. With 3 graphs.

During the year 1929 the scheme of dosage was modified. Cords dried 0 and 1 day were introduced and the total dosage was increased. As a result the mortality amongst those bitten by animals proved or suspected to be rabid fell from 1·43 (1,684 treated) to 0·78 per cent. (2,177 treated). "The treatment thus modified has no contra-indications, and does not cause serious inconvenience: paralyses remain practically unknown."

FUNAYAMA[22] summarizes the results of treatment at Kioto (Japan) during the eight years 1925 to 1932. During the period 923 persons have been treated by cords dried from 1 to 5 days; of these 4 developed the disease. No paralytic sequelae have been observed.

v. *Rabies in Animals.*

A further report on the results of vaccination of animals in Morocco is submitted by REMLINGER and BAILLY.[23] (For previous reports see this *Bulletin*, Vol. 22, p. 704, Vol. 26, p. 737, Vol. 27, p. 755, Vol. 30, p. 137). Ether vaccine was used as previously, and treatment was either prophylactic, after the bite, or for the maintenance of a previously established immunity. Of 1,624 animals inoculated (148 after being bitten) none contracted rabies.

The advantages of formol vaccine are again set forth by PLANTUREUX.[24] (See this *Bulletin*, Vol. 29, p. 195 and earlier reviews). The author emphasizes the importance of prophylactic vaccination of dogs in the control of rabies, and points out that with the use of a vaccine in which formalin (4 to 6 per thousand) is kept in contact with the emulsion for 7–14 days and then decanted off, no paralytic accident has been observed in the case of over 2,000 dogs. He states that "in our previous researches we incubated the vaccine at 37°C. in order to obtain a product which was entirely atoxic. Unfortunately, subjection to this raised temperature reduced the immunizing properties of the vaccine, and so we have had to omit this technique." In order to obviate this difficulty the author suggests that the vaccine be kept in contact with formalin for a longer time at a lower temperature. [As the effect of incubation upon the immunizing properties of vaccines killed by the action of any preservative—be it phenol, or be it formalin—is a point of great practical importance it is suggested that PLANTUREUX should publish the results of his experiments in detail.]

That the cat may transmit rabies is well known. REMLINGER and BAILLY[25] draw attention to the fact that in certain countries the number of persons bitten by cats is relatively high. They recommend prophylactic vaccination of cats, and state that contrary to common opinion the cat is easy to handle. No apparatus is necessary to hold it. With patience inoculation is easy.

---

[22] FUNAYAMA (Jun-Itchi). Résultats des vaccinations antirabiques pratiquées, de 1925 à 1932, au laboratoire antirabique de l'Université Impériale de Kioto.—*Ann. Inst. Pasteur.* 1934. Apr. Vol. 52. No. 4. pp. 473–477.

[23] REMLINGER (P.) & BAILLY (J.). La vaccination antirabique des animaux au Maroc en 1930.—*Arch. Inst. Pasteur d'Algérie.* 1931. June. Vol. 9. No. 2. pp. 333–341. [12 refs.]

[24] PLANTUREUX (E.). Avantages de la vaccination antirabique des chiens avant morsure dans la prophylaxie de la rage. Contribution à l'étude des accidents paralytiques et des moyens de les éviter.—*Arch. Inst. Pasteur d'Algérie.* 1933. Sept. Vol. 11. No. 3. pp. 513–521.

[25] REMLINGER (P.) & BAILLY (J.). Vaccination préventive du chat contre la rage.—*Bull. Acad. Méd.* 1933. Nov. 28. 97th Year. 3rd Ser. Vol. 110. No. 38. pp. 577–581.

vi. *Miscellaneous.*

OROPEZA[26] describes a case of human rabies in Venezuela, where in spite of the large number of stray dogs, the disease is rarely observed.

Successful efforts to control rabies in the district of Saigon-Cholon are discussed by LEBON.[27]

The biochemical characteristics of the blood of rabbits during the course of rabies infection are described by IIO.[28] The blood cholesterin diminishes slightly from the time of infection, but after some days it increases. There is no increase of sebaceous acids or of lecithin. There is no change in lipase content. A decrease in blood sugar when symptoms manifest themselves is followed by an increase in the later stages. The iodic acid index rises 10 to 30 per cent. but falls during the agony.

The total serum albumen diminishes, whilst globulin and fibrinogen increase. There is no change in water content. The rate of sedimentation of the erythrocytes increases. All these changes point to a destruction of albumen in the system.

FISHL[29] compares the results of treatment in Palestine by the Pasteur-Calmette and by the carbolized vaccines (incubated at 37°C.).

A pamphlet giving information and instructions regarding rabies and its treatment in India is written by SHORTT.[30] Its most striking feature is the evidence it affords regarding the extent to which the treatment has been decentralized. For example in the Madras presidency the number of treatment centres is 115, 33 centres are served by the Shillong Institute, and 44 by the Institute at Bombay. Also a new Pasteur Institute has been opened at Patna which will deal with patients from Bihar and Orissa.

In an article of 29 pages, GONZALEZ[31] deals with the whole subject of rabies: its history, its manifestations, and its treatment. To this is added a summary of the results of treatment at the institutes at Buenos Ayres and La Plata. The article concludes with a discussion of paralytic accidents, and of methods of prophylaxis.

HAGUENAU, CRUVEILHIER and NICOLAU[32] claim that antirabic vaccination (15 days, cords dried from 2 to 5 days), gives favourable results in the treatment of sciaticas, migraine, and certain painful tabetic conditions. *A. G. McKendrick.*

---

[26] OROPEZA (Pastor). Un caso de rabia humana.—*Gac. Med. de Caracas.* 1933. Oct. 31. Vol. 40. No. 20. pp. 286–287.

[27] LEBON. De la lutte contre la rage dans la région de Saigon-Cholon durant les années 1931–1932–1933.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1933, Nov.–Dec. Vol. 11. No. 8. pp. 1040–1047. With 4 figs.

[28] IIO. Etude biochimique du sang chez les lapins enragés.—*Oriental Jl. Dis. Infants.* 1933. Nov. Vol. 14. No. 3. [In Japanese. French summary pp. 67–69.]

[29] FISHL (Moshe). The Methods of Anti-Rabies Treatment in Palestine.—*Harefuah.* 1933. Sept.–Oct. Vol. 7. No. 5. [In Hebrew pp. 212–228. English summary pp. 1–2.]

[30] SHORTT (H. E.). Rabies and Anti-Rabic Treatment in India. Information and Instructions for Anti-Rabic Treatment.—50 pp. 1933. Delhi.

[31] GONZÁLEZ (Hernán D.). La rabia humana.—*Semana Méd.* 1934. Apr. 26. Vol. 41. No. 17 (2102). pp. 1244–1275.

[32] HAGUENAU (J.), CRUVEILHIER (L.) & NICOLAU (S.). Sur l'emploi du virus-vaccin antirabique dans le traitement de certaines algies et de la migraine.—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1934. May 21. 50th Year. 3rd Ser. No. 16. pp. 671–680.

AMOEBIASIS AND DYSENTERY.

Amoebiasis.

Reed (Alfred C.) & Johnstone (Herbert G.) with the Technical Assistance of Jeanette Van Dalsem Anderson. **Amebiasis among One Thousand Prisoners. Final Report.**—*Amer. Jl. Trop. Med.* 1934. Mar. Vol. 14. No. 2. pp. 181–189. [11 refs.]

This report summarizes the results of a protozoologic survey of 1,000 inmates of San Quentin Prison (California) together with treatment of positive amoebiasis cases and a follow up of treated cases.

Examination of stools was by the wet fixation smear and iron-haematoxylin staining technique. 9·2 per cent. of the 1,000 examined were found infected with *E. histolytica.* These were treated with vioform and carbarsone, and were subjected to a careful follow up of more than 16 months, during which chances for reinfection were minimal. Ninety per cent. remained free of *E. histolytica* during this follow up period. On these observations the authors found a belief that re-infection is more important than relapse and that the chief spread of amoebiasis is by food handlers. *H. M. Hanschell.*

Mackie (Thomas T.) & Nauss (Ralph W.). **Familial Infection by *Endamoeba histolytica* in New York City. Preliminary Report.**—*Amer. Jl. Trop. Med.* 1933. Nov. Vol. 13. No. 6. pp. 577–582. [15 refs.]

Report of observations made on a family of six, resident in New York City, four members of which were found infected with *E. histolytica.* The infection was probably acquired by one parent outside the city and transmitted to the children. Such a family infection occurring under good living conditions emphasizes importance of searching for and adequately treating carriers of *E. histolytica.*

H. M. H.

Hegner (Robert). **Transmission of *Endamoeba histolytica* in Drinking Water.**—*Jl. Parasitology.* 1934. Mar. Vol. 20. No. 3. p. 199.

The author records observations which appear to support the contention, often disputed, that drinking water may be a habitual source of infection with *E. histolytica.* Many missionaries in a Mission in Chiquimula, Guatemala, had during the past decade suffered from severe attacks of amoebic dysentery; during the year following installation of a pure drinking water supply no cases of dysentery had occurred.

H. M. H.

Heatly-Spencer (J.). **Difficult Diagnoses. I.—Minor Manifestations of Amoebiasis with a Note on their Diagnosis by the Differential Blood-Count.**—*Jl. Roy. Army Med. Corps.* 1934. Feb. Vol. 62. No. 2. pp. 81–84.

In what may be called the lesser hepatic cases of amoebiasis there may be utmost difficulty in arriving at correct diagnosis, for often none of the usual signs and few of the symptoms of hepatitis are present. In such cases, the author claims, the Schilling-Torgau differential blood count (modification of the Arneth index) is a powerful aid to diagnosis.

The Schilling index does not pick out amoebiasis and declare it, but it does tell when a pathological condition of the blood secondary to an inflammatory process is, or is not, present. Details of two cases of "hepatitis" are given in illustration of the significance of the Schilling index.

The first case presented all the classical symptoms and signs of severe hepatitis following one year after successful surgical treatment of tropical liver abscess.

Blood counts were :—

	Normal (for comparison)	Case on admission	After 1 week's treatment	After 2 week's treatment
Total count ...	... ...	21,000	20,400	13,000
Differential	Per cent.	Per cent.	Per cent.	Per cent.
Eosinophils	3	nil	2	2
Lymphocytes	23	12	15	22
Myelocytes	nil	nil	nil	nil
Metamyelocytes	nil	2	1	1
Band forms	4	30	10	6
Polymorphonuclears ...	63	54	64	64
Large mononuclears and transitionals	6	2	7	4
Mast-cells	1	—	1	1
	100	100	100	100

Before commencement of treatment the count shows, in the acute stage of illness, a marked shift to the left illustrated by the rise of band form granular cells, the fall of lymphocytes, and the low relative total of polymorphonuclears. After two weeks' treatment there has been an almost complete change back to a normal differential count. The lag behind of the total count caused no anxiety in view of the recovery of the differential count.

The next case illustrated is one of those in which diagnosis by physical means was impossible. The patient complained of general unfitness with vague sensations of discomfort in region of liver, increased at times by some jarring movement. Investigation revealed nothing—nor did X-ray. The total leucocyte count was good.

Differential count :—

Eosinophils	6 per cent.	Polymorphonuclears	38 per cent.
Lymphocytes ...	32 ,,	Large mononuclears	4 ,,
Metamyelocytes ...	14 ,,	Mast cells ...	1 ,,
Band forms ...	4 ,,		

The significance of this count lay in the 14 per cent. metamyelocytes, precursors of the band forms of granular leucocytes. Here then was a definitely pathological count indicating an inflammatory process. Two weeks after treatment, the patient being well on the way to recovery, the count read :—

Eosinophils	6 per cent.	Band forms ...	nil
Lymphocytes ...	41·8 ,,	Polymorphonuclears	47 per cent.
Metamyelocytes ...	2·8 ,,	Large mononuclears	2·4 ,,

Important significance lies in the finding of immature polymorphonuclears either in excessive numbers in band forms, or in the appearance of the definitely pathological earlier forms known as metamyelocytes or myelocytes. *H. M. H.*

NGAI (S. K.) & FRAZIER (C. N.). **Cutaneous Amoebiasis. A Review and Report of Three Cases observed in North China.**—*Chinese Med. Jl.* 1933. Nov.–Dec. Vol. 47. Nos. 11 & 12. pp. 1154–1170. With 6 figs. on 4 plates. [30 refs.]

This paper gives a careful review and discussion of twenty-seven cases of amoebiasis cutis reported since 1891 and in addition a detailed clinical and parasitological and histological report of three cases observed in Peiping.

The authors state that cases of cutaneous amoebiasis in which the organism has been studied and identified as *E. histolytica* are few in number. In general they fall into two clinical groups: those in which the dermatitis is secondary to an amoebic abscess of the abdominal viscera, usually the liver; and those with fistulous or condylomatous ulcers of the perianal region and buttocks. Adequate study has not been made of the source of infection especially in the latter group, but it is assumed to be an antecedent amoebic colitis with or without symptoms of dysentery. In the former group involvement of skin is by direct extension of an abscess or along a surgical incision; in the second group presumably by direct contact with contaminated faeces, or by direct extension from the bowel.

Of the authors' three cases, here described, two showed condylomatous lesions of the genito-anal region, one of which was preceded by an acute bloody diarrhoea. One case, that of a woman, was complicated by early syphilitic disease of the genitalia. In the third case a papilloma of the anal region was invaded secondarily by *E. histolytica*.

The amoebae were studied in fixed tissue preparations (biopsy) in each case, and in the living form in one, and identified as *E. histolytica*. The histological characteristics of the skin lesions were like those produced in other tissues by this parasite. The presence of amoebae between fairly normal epithelial cells in the most superficial lesions and their tendency to spread along the path of least resistance in deeper structures suggest that the amoeba may be able to penetrate tissue by the mechanical action of its pseudopodia. *H. M. H.*

CRAWFORD (Stanley). **Amebiasis Cutis: Report of a Case.**—*Arch. Dermat. & Syph.* 1933. Sept. Vol. 28. No. 3. pp. 363–368. [19 refs.]

The author gives a full report of a case of extensive amoebic ulceration of both buttocks, which began as an amoebic abscess in the perianal region in association with amoebic colitis. After rupture of the abscess the ensuing ulceration of skin (biopsy revealed *E. histolytica* invading the cutis) spread over both buttocks during a period of four years, leaving tough fibrous scars in healed areas, while active areas persisted peripherally in spite of treatment with emetine hydrochloride and excision. *H. M. H.*

CHOPRA (R. N.), SEN (S.) & SEN (B.). **Treatment of Chronic Intestinal Amoebiasis with Gavano, a Derivative of Ipecacuanha.**—*Indian Med. Gaz.* 1934. Mar. Vol. 69. No. 3. pp. 130–133.

The authors record the results of treatment by gavano in 18 cases of chronic amoebic dysentery.

The criterion of cure, the only one possible in the circumstances, was six negative examinations after cessation of treatment. Six patients were cured, in 10 the drug failed and in 2 results were indeterminate, the proportion of probable cures to failures in this series being 1 : 1·66.

The drug was given by mouth. It is claimed to be a derivative of ipecacuanha, and to be a compound of emetine or cephaeline with an organic acid. In therapeutic doses it causes no vomiting or nausea, has no irritant effect on kidney or liver, and no toxic effect on circulatory and nervous systems, but its amoebicidal properties appeared to be less than those of E.B.I., the kurchi alkaloids, or carbarsone.

Neither kurchi alkaloids nor carbarsone, two of the most effective drugs against chronic amoebiasis, have any effect on liver conditions associated with amoebiasis. It is possible that gavano or an allied compound may prove a less toxic drug than emetine for such conditions. *H. M. H.*

ANDERSON (Hamilton H.). **Emetin in Amebiasis.**—*California & Western Med.* 1934. Mar. Vol. 40. No. 3. pp. 198–199.

The author protests that since less toxic and more effective amoebicides are available, one should not embarrass an infected individual by using such a potentially dangerous drug as emetine except in those cases exhibiting impaired hepatic function or hepatic abscess.

It has been demonstrated experimentally and clinically that emetine is many times more toxic when given by vein than by mouth, subcutaneously or intramuscularly. Even oral administration results in accumulation of the drug in the body. The subcutaneous route is the method of choice, however, for emetine may cause disturbed gastroenteric function when given by mouth. Abscess may result from its injection into muscle. Excretion of the drug is extremely slow. It is apparently fixed in muscle tissue, particularly cardiac, and on this account toxic range for repeated doses is the same as for a single administration. Pathologic and cardiographic evidence support JAMES's contention that patients who have been given emetine are not good surgical risks because of possible myocardial damage resulting from the drug. Clinically an increase in pulse rate and lowering of blood pressure indicate beginning of cardiac dysfunction. Abnormal cardiographic tracings are obtained only in patients who have severe myocardial involvement. *H. M. H.*

CHOPRA (R. N.) & SEN (B.). **Toxic Effects of Emetine on the Cardiovascular System.**—*Indian Med. Gaz.* 1934. May. Vol. 69. No. 5. pp. 262–263. With 1 fig.

The case of a European woman of 48 admitted to the Carmichael Hospital for Tropical Diseases with general irritation of the skin and feeling of weakness and depression. Four years before she was treated

in London for amoebic dysentery receiving a course of emetine-bismuth-iodide by the mouth for 12–14 days; after 6 daily doses the pulse became rapid and the patient extremely weak and she was kept in bed for 7 days. She regained health in about a month and returned to India. In 1933 she had an attack of amoebic dysentery and was put on emetine. After 9 injections (6 on successive days, then on alternate days), she became very weak with frequent pulse, mental depression and itching skin. Three weeks later she came under the authors' care. The pulse was then 90 to 100, of low tension, the blood pressure 106 mm. systolic and 70 mm. diastolic. No urticaria; no helminths or protozoa in the stools; no malarial parasites. Electro-cardiographic examination (curves and data given) indicated myocardial damage with tachycardia of sinus origin.

The authors point to the toxic effect of emetine on both occasions. Colonel Chopra has seen several cases in which itching of the skin and even urticaria and large pruriginous plaques were produced and persisted for a month after a course of emetine, which damages the capillaries. He published a paper in 1924 on the changes in the hearts of rabbits after emetine administration [see this *Bulletin*, Vol. 21, p. 916]. *A. G. B.*

Bacillary Dysentery.

de Assis (Arlindo). Dysenteria bacillar. A proposito de sua etiopathogenia. [**Bacillary Dysentery.**]—*Brasil-Medico.* 1934. May 5. Vol. 48. No. 18. pp. 308–313. [10 refs.]

In this review of bacillary dysentery, as it occurs in Brazil, there are one or two observations to note with regard to the organisms which have been isolated in epidemic and endemic dysentery. The organisms are:—(1) The bacillus of Shiga (2) the bacilli of the group of Flexner, containing such types as Strong, Y and Hiss, (3) the bacillus of Schmitz closely resembling the Shiga bacillus and mannite-negative but easily distinguishable by its indologenic power and its serological specificity, and (4) the bacillus of Sonne, often called Kruse-Sonne and which should strictly be called the Castellani-Kruse-Sonne bacillus.

Some reference is made to the gravity of clinically acute cases according to the causative type of organisms. These are arranged as follows:—(1) Cases of moderate or severe symptoms with varying prognosis, but usually good, due to bacilli of Shiga and of Flexner-Hiss, (2) well defined cases of moderate or severe symptoms but of short duration and good prognosis, due to the bacillus of Schmitz, and (3) doubtful clinical cases resembling more dysenteriform enteritis of subacute type, of quite good prognosis, due to the Sonne bacillus.

Some observations are made on the "healthy carrier," and the opinion is expressed that such carriers are cases of dysentery of trivial type and perhaps of isolated and trivial lesions. They may, however, progress.

Dysenteries may be divided clinically into two types, the acute, classical, unmistakable dysentery, and the chronic dysentery which may not always be diagnosable as true dysentery and is liable to be confounded with localized disturbances in the intestinal tract.

W. F. Harvey.

CHOPRA (R. N.) & CHAUDHURI (R. N.). **Dysentery produced by** *Bacterium pseudo-carolinus.—Indian Med. Gaz.* 1934. May. Vol. 69. No. 5. pp. 251–254.

Bacteriologists have been familiar now for nearly three decades with a multitude of organisms, all named, and all supposed to have etiological relationships to dysentery. Probably the naming adopted by KRUSE, which gave to each new bacillary form, as it emerged, a new letter of the alphabet, was the simplest and best. After him many an organism has appeared, with an eponymous title, to claim a place upon the dysentery string. Many of these have had to forego their place as new entities because of proofs of identity with one or other of KRUSE's alphabetical series. There is presented in this article a very good case for the causation of a more or less type form of dysentery by *Bacterium pseudo-carolinus*, a type quite capable of being recognized through its syndrome by an acutely observant nursing sister. "The number, colour and consistency of the stools passed was very variable in different cases. The stools were either diarrhoeic or constipated, pasty looking or hard; they had a more or less normal yellow coloration or were clay coloured. There was both blood and mucus in the stools in seven patients only, while the large majority, *i.e.*, 24 cases, had neither blood nor mucus in the stools while in hospital." *Bacterium pseudo-carolinus* is not a lactose fermenter and produces not merely acid but gas in glucose, maltose and mannite. But by far the most interesting and possibly important observation made by the authors is the suggestion that this organism may be no more than a variant of *Bact. flexneri* produced by the action of a phage, "phage-mutated" is the expression used. It would be a great simplification if a number of the present competing non-Shiga, "pseudo-dysentery" species could be reduced to variants, by dissociation or phage action, of a few simple stem forms.

W. F. Harvey.

GUNEWARDENE (T. H.). **Acute Bacillary Dysentery in Children: Advantages of its Treatment by Petroleum and Allied Preparations.** *—Indian Med. Gaz.* 1934. May. Vol. 69. No. 5. pp. 256–259. With 1 chart.

Much of this article is taken up with the symptomatology, diagnosis, prognosis and treatment of acute dysentery in children. The point of special interest is the treatment adopted. The treatment preferred is by liquid petroleum-nujol in half drachm doses every 2 hours while the child is awake. Hydrolax may be used in older children. No purgatives and no intestinal antiseptics are required. It is suggested that the nujol acts like natural mucus. With this treatment children "show marked improvement sooner than when treated by active purgation." Symptoms such as extreme restlessness due to dehydration, irritation and tenesmus, are greatly diminished or are not manifest at all.

W. F. Harvey.

DE MENDONÇA (F. Carneiro). Ueber die Endemie der Dysenterie in der Irrenanstalt in Rio de Janeiro. [**Endemic Dysentery in the Lunatic Asylum, Rio de Janeiro.**]—*Deut. Med. Woch.* 1934. May 25. Vol. 60. No. 21. pp. 794–795.

Endemic dysentery in the Rio de Janeiro lunatic asylum is bacillary and due especially to organisms of Flexner type. Its continuance has

been traced to carriers and its transmission to flies. The administration of serum by the mouth and measures against flies were followed by disappearance of the endemic. *W. F. Harvey.*

BOYERS (Luther Musson). Human Amebiasis. A Review of 700 Cases expressing 1961 Complaints.—*California & Western Med.* 1933. Dec. Vol. 39. No. 6. pp. 397–401.

DE BUEN (Sadi). Sobre un caso de disenteria amebiana.—*Medicina Países Cálidos.* Madrid. 1934. Apr. Vol. 7. No. 4. pp. 145–149. With 8 figs. [12 refs.]

FERNAN-NUNEZ (M.). Amebiasis: its Clinical Aspects and Control.—Reprinted from *Wisconsin Med. Jl.* 1934. Mar. 5 pp.

FOSTER (John H.). Amebiasis in Connecticut.—*New England Jl. of Med.* 1934. Feb. 8. Vol. 210. No. 6. pp. 294–299. With 4 figs. [11 refs.]

GRADWOHL (R. B. H.). Diagnosis of Amebiasis. [Correspondence.]—*Jl. Amer. Med. Assoc.* 1934. Jan. 6. Vol. 102. No. 1. pp. 65–66. With 1 fig.

HUARD (P.). Aspects chirurgicaux de l'amibiase coecocolique avec neuf observations personnelles.—*Marseille-Méd.* 1933. Nov. 15. Vol. 70. No. 32. pp. 549–585. [7 pages of refs.]

HUARD (P.), ROQUES (P.) & DEJOU (L.). Double abcès du lobe hépatique droit, compliqué d'abcès sousphrénique, d'abcès pulmonaires et de péricardite suppurée, sans perforation diaphragmatique.—*Marseille-Méd.* 1933. Sept. 15. Vol. 70. No. 26. pp. 293–308. With 3 figs.

IKEDA (Kano). Unusual Experience with Amebic Dysentery in an Average Hospital of a Northern State, with Report of Nine Cases originating in Chicago.—*Jl. Amer. Med. Assoc.* 1933. Dec. 16. Vol. 101. No. 25. pp. 1944–1953. With 6 figs.

McCOY (G. W.). Amoebic Dysentery. Problems presented by the Outbreak in 1933.—*Public Health Rep.* 1934. Feb. 2. Vol. 49. No. 5. pp. 141–144.

REED (Alfred C.). Amebiasis—a Clinical Summary.—*California & Western Med.* 1934. Jan. Vol. 40. No. 1. pp. 6–10.

STILL (R. M. Lloyd) & DANG (Manohar Lal). A Case of Resistant Protozoal Dysentery.—*Indian Med. Gaz.* 1934. Feb. Vol. 69. No. 2. pp. 82–83.

SUMERLIN (H. S.). Amebiasis. Incidence in Private Practice.—*Jl. Amer. Med. Assoc.* 1934. Feb. 3. Vol. 102. No. 5. pp. 363–364.

KALA AZAR.

BOGLIOLO (Luigi). Studi sulle leishmaniosi. I. Lo stato attuale delle conoscenze sulla trasmissione delle leishmaniosi. [**Present State of Knowledge of the Transmission of the Leishmaniases.**]—*Ann. di Med. Nav. e Colon.* 1934. Mar.–Apr. 40th Year. Vol. 1. No. 3–4. pp. 139–213. [204 refs.] German summary.

This article which was completed in June 1933 is similar to several others which have appeared during the past few years and reviews in a critical manner all the work which has been done on the transmission of the various forms of leishmania infection.

The author, who has not himself worked at the problem, comes to the conclusion, as a result of his perusal of the literature, that the method of spread is still unknown. Though the article contains no new information it is useful as a guide to the now extensive literature dealing with the subject. Over 200 articles are mentioned in the references. *C. M. Wenyon.*

FORKNER (Claude E.) & ZIA (Lily S.). **Viable** *Leishmania donovani* **in Nasal and Oral Secretions of Patients with Kala-Azar and the Bearing of this Finding on the Transmission of the Disease.**—*Jl. Experim. Med.* 1934. Apr. 1. Vol. 59. No. 4. pp. 491–499.

The authors have discovered leishmania in the material obtained by passing an ordinary swab over the nasal mucosa of nine kala azar patients. Parasites were also seen in the material blown from the nose.

In one of the cases they were also found in smears from the tonsil and in the saliva. The tonsil of this patient was found to be heavily infected when sectioned after death. The nasal discharge from two of the cases produced infection in hamsters by intraperitoneal inoculation. The number of parasites in the nasal smears varied. In some they were easily found, in others with difficulty. Two human volunteers and numerous animals have been inoculated into the nasal and oral cavities with nasal discharge containing leishmania, but the results are not yet evident. *C. M. W.*

MORALES GONZALEZ (Juan L.). Nota epidemiologica sobre el kala-azar en la provincia de Sevilla. [**K.A. in the Province of Sevilla.**]—*Medicina Países Cálidos.* Madrid. 1934. Jan. Vol. 7. No. 1. pp. 19–25. With 1 map. French summary (4 lines).

Since the discovery of the first case of infantile kala azar in the province of Sevilla in Spain in 1915 about 15 fresh cases have been identified. Of these 5 were noted during the next 14 years and the rest since then. It appears that not only is the disease endemic in the province but it has been on the increase during the past 3 years.

C. M. W.

MENDES (A. B. Corrêa) & FERREIRA (J. Chaves). Kala-azar infantil em Alcacer do Sal. [**Infantile K.A. in Alcacer do Sal, Portugal.**]—*Arquivos Inst. Bact. Camara Pestana.* 1933. Vol. 7. No. 1. pp. 113–129. With 1 map, 4 figs. & 3 charts. English summary.

During the course of anti-malaria work at Alcacer do Sal in Portugal the authors encountered 11 cases of infantile kala azar amongst attendants at the dispensary during the period October 1932 to January 1933.

The ages varied from 7 months to 8 years, the highest incidence being at 2 years (5 cases). All were diagnosed by spleen puncture and all, except one child who was *in extremis* when first seen, were successfully treated by intramuscular injections of neostibosan (0·05 to 0·20 gm.) given every two days. The total dose varied from 1·25 to 1·90 gm. according to age. In some cases to ensure a cure it was necessary to repeat the course. No further cases of the disease have been seen at the dispensary. *C. M. W.*

D'OELSNITZ. Valeur sémiologique des manifestations ganglionnaires et spécialement des adénites épitrochléennes du kala-azar. [**Diagnostic Value of Enlargement of Glands, Especially the Epitrochlear, in K.A.**]—*Bull. Acad. Méd.* 1934. May 8. 98th Year. 3rd Ser. Vol. 111. No. 17. pp. 619–620.

During his 10 years experience of kala azar in children and adults in the south of France the author has come to recognize a general glandular enlargement, in which the epitrochlear glands are especially involved and much more enlarged than other glands, as a sign of kala azar, provided always that syphilis can be excluded. *C. M. W.*

NATTAN-LARRIER (L.) & GRIMARD-RICHARD (L.). Sur le séro-diagnostic de la leishmaniose viscérale. [**The Serodiagnosis of Visceral Leishmaniasis.**]—*C. R. Soc. Biol.* 1934. Vol. 115. No. 3. pp. 266–269.

In this paper the authors give some further details of the method of carrying out the serological test which they have described for the diagnosis of leishmania infections (*ante*, p. 230). From their further experience of the test they confirm their original conclusion that it is the diagnostic method of choice when it is not possible to undertake spleen or other puncture for the discovery of parasites.

C. M. W.

CAMINOPETROS (J.). Une séro-floculation spécifique de la leishmaniose interne. Son utilité pour le diagnostic de l'infection et pour le contrôle du traitement. [**A Specific Sero-flocculation in K.A. Its Value in Diagnosis and Treatment.**]—*C. R. Soc. Biol.* 1934. Vol. 115. No. 9. pp. 910–912.

If to 2 cc. of a 1 to 4 per cent. aqueous solution of sulfarsenol is added drop by drop serum of a case of kala azar it will be found that after the addition of the first drop a milky colour is produced. This increases in intensity and becomes a definite flocculation when 7 to 20 drops have been added. The addition of more drops after the maximum flocculation has been reached causes it to diminish and finally disappear.

With sera from healthy individuals or from those with diseases other than kala azar the slight flocculation which may be produced at the first drop has completely disappeared by the third or fifth. If to the solution of sulfarsenol to be used are added 3 or 4 drops of a serum

which is known not to give the flocculation this will prevent the reaction with kala azar sera. The reaction appears very early in kala azar infections and does not disappear till a definite cure has resulted. The author claims that the test is more reliable than the antimony test.

C. M. W.

SANCHIS BAYARRI (V.) & MONTOLIU VOLANT (C.). Nueva tecnica para el diagnostico serologico del kala-azar. [**New Technique for the Serodiagnosis of Kala Azar.**]—*Medicina Países Cálidos.* Madrid. 1934. Jan. Vol. 7. No. 1. pp. 12–18. French summary (6 lines).

In carrying out the antimony test for kala azar the authors advise the use of a 4 per cent solution of urea stibamine in physiological saline and a 1 in 5 and 1 in 10 dilution of the serum, which has previously been heated to 56°C. for half an hour. The precipitate obtained at the point of contact of the solution and serum is a very definite one, the reaction being absolutely specific for kala azar. *C. M. W.*

D'OELSNITZ (M.) & RONCHÈSE (A. D.). Valeur et sensibilité de la réaction de Chopra pour le diagnostic du kala-azar. [**Value and Sensitivity of Chopra's Reaction for the Diagnosis of K.A.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1934. Apr. 30. 50th Year. 3rd Ser. No. 13. pp. 548–553.

During 3 years the authors have tested the antimony reaction in cases of kala azar in the south of France.

The best results have been obtained by pouring on to the surface of the undiluted serum a 4 per cent. solution of urea stibamine. The precipitate formed with the serum of cases of kala azar is of a tenacious character, not broken up by shaking and sinking finally to the bottom of the tube as a compact mass. If, as sometimes happens, sera from other cases give a slight cloud at the surface of contact this disappears spontaneously in the course of half an hour. With old solutions a more definite precipitate may form but this dissociates rapidly into minute flocculi which sink to the bottom. These false reactions cannot be confused with the genuine one. It has been found that urea stibamine gives a better result than neostibosan, while undilute serum and a solution of the drug not stronger than 5 per cent. gives better reactions than other concentrations. Though fresh solutions should be used if possible, serum nine months old and solutions of the drug kept sterile in ampoules for 18 months are still capable of giving a reliable test. The authors state that the only cause of error is the patient having taken quinine. Compared with the formol-gel test the antimony reaction of CHOPRA is both more rapid and reliable and remains the most satisfactory of completely safe tests for the identification of kala azar.

C. M. W.

KASSIRSKY (I. A.). Die Punktion des Knochenmarkes und die Blutbildung bei der visceralen Kinderleishmaniose. [**Bone Marrow Puncture and Blood Formation in Infantile K.A.**]—*Folia Haematologica.* 1934. Mar. Vol. 51. No. 3/4. pp. 352–358. With 2 figs.

In this paper the author reverts to the subject of puncture of the sternum for the diagnosis of kala azar in children (*ante*, p. 231) which he

claims to be not only a safer and simpler operation than spleen puncture but one which is more accurate in its results. The opportunity was taken of studying the material obtained from the point of view of the changes which occur in the marrow cells in the course of the disease.

It is concluded that there occurs an increased erythrocyte destruction. This is borne out by the slight jaundice, the presence of indirect bilirubin up to 1 in the serum and the increase in the urobilinuria and osmotic resistance of the erythrocytes. In response to this the bone marrow produces more red cells as also do extramedullary centres of blood regeneration which come into operation. The red cell destruction occurs in the spleen, liver and other places where the reticulo-endothelial system is hypertrophied. It is probable that the red cells are also affected to some extent by the action of a toxin from the parasites, as evidenced by their abnormal size and shape. In the peripheral blood the regenerative process produces polychromatophilia and the presence of normoblasts to the number of 2 to 3 to 100 leucocytes. In the white parts of the marrow in early stages of the disease when there are 6,000 to 9,200 leucocytes in the peripheral blood there may be a marked reaction in the direction of premyelocyte production. When, however, the stage of leucopenia supervenes the marrow responds with the myeloid reaction. It is then possible to distinguish degenerative changes in the marrow leucocytes. The eosinophile cells are frequently present in the marrow in greater numbers than in the blood, a feature which the author thinks is indicative of a good prognosis. Of especial interest is the presence in the marrow of large numbers of lymphocytes (25 to 30 per cent.), but it is believed that the majority of these at least are brought to the marrow by the blood, where they may form 80 per cent. of the total leucocytes. On the other hand it cannot be denied that some lymphocyte production may occur in the marrow. Another cell in the material is the monocyte, the origin and development of which can be studied to advantage. It is clear that the investigation of marrow obtained in the way described is capable of throwing considerable light on the processes of blood destruction and regeneration and the cellular response to leishmania and other infections. *C. M. W.*

INDA (Francisco F.), VÍVOLI (Donato) & VACCAREZZA (Américo J.). Estudio anátomo-clínico de un caso de kala-azar en el adulto (fiebre negra). Primera observación en nuestro país. [**K.A. in an Adult, seen in Argentine.**]—*Semana Méd.* 1934. Feb. 8. Vol. 41. No. 6 (2091). pp. 413–424. With 5 figs.

The case described is that of a man 34 years of age who emigrated to the Argentine from Yugoslavia in 1929. He commenced to be ill in 1931, a year and a half after taking up his residence in the district of Salta. The disease developed during the next year till in a serious condition he was admitted to hospital on October 26, 1932, and died a few days later. Examination of the organs *post-mortem* revealed a leishmania infection. Though the district of Salta is known to be an endemic centre of cutaneous leishmaniasis the authors incline to the view that the case was one of kala azar contracted in the Mediterranean region by the patient before he left for the Argentine. Clinically and pathologically the case appears to have been a typical one of this disease. *C. M. W.*

BENELLI (C.), ZUCCARELLI (J.) & SAUTET (J.). A propos d'un cas Corse de kala-azar de l'adulte à évolution fatale. [**A Fatal Case of K.A. in a Corsican Adult.**]—*Rev. Méd. et Hyg. Trop.* 1933. Sept.–Oct. Vol. 25. No. 5. pp. 261–262.

The case described was in an adult 23 years of age. The disease, contracted in Corsica, had been diagnosed as kala azar two years before this and a course of neostibosan injections given. After the course nothing was heard of the patient till his return to the hospital two years later in a condition of extreme cachexia. The original diagnosis was confirmed by the discovery of parasites by spleen puncture. Death resulted shortly after in spite of treatment. *C. M. W.*

EAST AFRICAN MEDICAL JOURNAL. 1934. Mar. Vol. 10. No. 12. pp. 363–364.—**A Case of Kala Azar from the Elgeyo Reserve.**

The case of kala azar recorded was in a native of the country and is the first autochthonous case to be diagnosed in Kenya by the discovery of leishmania by spleen puncture. In 1927 a case was identified on clinical grounds alone, but the present case recognized by Dr. FORBES proves that the disease exists in Kenya. It is pointed out that the population of the Elgeyo reserve has increased very slowly during the past four years, and that kala azar may be responsible for this. Cases of cutaneous leishmaniasis were recorded in Kenya in 1931 and 1932.

C. M. W.

GIBSON (P. L.) & O'FLYNN (J. A.). **A Case of Kala-Azar.**—*Jl. Roy. Nav. Med. Serv.* 1934. Apr. Vol. 20. No. 2. pp. 184–185.
JOURNAL OF THE ROYAL NAVAL MEDICAL SERVICE. 1934. July. Vol. 20. No. 3. p. 266.—**Additional Note to a Case of Kala-Azar. Reported on p. 184 of the April, 1934, Issue of this Journal.**

The case of kala azar described was in a naval rating who contracted the disease in Malta. The Wassermann test, which was negative on March 30 and October 12, 1933 showed on January 19, 1934 full inhibition of haemolysis in the test and also in the control (no antigen) tube. It is suggested that the factor responsible for the formol-gel reaction, which was strongly positive in this case, may have been the cause of the deviation of the complement and may account for the records of positive Wassermann reactions in some cases of kala azar.

C. M. W.

GIRAUD (Paul), MOLLARET & MONGES (F.). Trois cas de splénomégalie chez l'adulte. Guérison par le traitement stibié. [**Three Cases of Adult Splenomegaly cured by Antimony Treatment.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1934. Apr. 2. 50th Year. 3rd Ser. No. 11. pp. 468–473. With 1 chart.

The authors describe 3 cases of splenomegaly seen by them in the south of France. All three appeared clinically to be kala azar and were cured by neostibosan or urea stibamine.

It is noted that in kala azar areas it is justifiable to suspect the disease and to proceed with appropriate treatment even when the final diagnosis by discovery of leishmania has not been made. It is pointed out that spleen puncture was not carried out in the last two of these cases because of a death which had followed this operation a short time

before. In the discussion following the paper DECOURT remarks that he had seen a case of kala azar in Paris in an adult who had made a stay on the Côte d'Azur. *C. M. W.*

D'OELSNITZ. Le kala-azar met-il les sujets atteints en état d'anergie ? [**Does K.A. cause Anergy ?**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1934. Mar. 19. 50th Year. 3rd Ser. No. 9. pp. 409–410.

A child from a tuberculous family in the south of France and giving a positive tuberculin skin test was admitted in June 1932 to a sanatorium situated in a large park away from outside contacts. With 50 other children the child in question remained in good health for 15 months, when it became ill. Finally kala azar was diagnosed and treated successfully with urea stibamine. It is recorded that the tuberculin test became negative with the development of kala azar but was positive again after cure. This appears to indicate that kala azar is able to bring about a condition of anergy which disappears when cure has taken place. The author remarks that the development of kala azar in the isolated situation in this single child shows what obscurity surrounds the method of transmission of this disease.

C. M. W.

NAPIER (L. Everard) & GUPTA (C. R. Das). **Further Clinical Observations on Post-Kala-Azar Dermal Leishmaniasis.**—*Indian Med. Gaz.* 1934. Mar. Vol. 69. No. 3. pp. 121–130. With 10 figs.

In this paper the authors revert to the subject of post-kala-azar dermal leishmaniasis which has been described by them and by ACTON and NAPIER in previous papers (this *Bulletin*, Vol. 25, p. 70 and Vol. 28, p. 160). The present paper deals with a series of 209 cases seen during the past 3 years and brings to a total of over 500 the cases seen in Calcutta, Assam and Madras.

In the present series all the clinical types previously described, with the exception of the " xanthoma " type, have been represented. Other types have come to light, such as mucous membrane lesions, small ulcerated cutaneous lesions, extensive erythema, peri-onchyial induration. It is clear that new types of lesion will be encountered from time to time and no claim is made that the types already seen represent limits of the forms the disease may assume. Further experience seems to show that the depigmented and erythematous lesions are not necessarily, as they were in the earlier reports supposed to be, the first lesions to appear and that they subsequently developed into nodules. There is some suggestion that in certain cases the lesions do not pass through the various stages of development indicated before. The presence of ulcerated lesions on the skin or mucous membrane of some cases does not in any way alter the conception of the disease as essentially a non-ulcerating one nor does it bring the condition into line with either oriental sore or muco-cutaneous leishmaniasis of South America.

C. M. W.

NAPIER (L. Everard) & SMITH (R. O. A.). **Dermal Leishmaniasis in Assam.**—*Indian Jl. Med. Res.* 1934. Jan. Vol. 21. No. 3. pp. 557–561.

Owing to the fact that a careful investigation in Madras had shown that the supposed absence or rarity of cases of post-kala-azar dermal

leishmaniasis was not correct, it was considered advisable to carry out a similarly careful survey in Assam, about which similar claims had been made. A careful inspection of villages and tea gardens where many cases of kala azar had been treated brought to light only a few cases of the skin infection. It seems, therefore, that in Assam, where kala azar has in recent years been present in epidemic form, the incidence of the dermal condition is very much lower than in Bengal and Madras, where there is a much better balance between host and parasite.

C. M. W.

BRAHMACHARI (Phanindranath). **Studies in Dermal Leishmanoid. Part I. Rare Type of Dermal Leishmanoid.**—*Jl. Trop. Med. & Hyg.* 1934. Mar. 1. Vol. 37. No. 5. pp. 68–70. With 2 figs.

The paper describes a rare type of dermal leishmanoid in 2 brothers, both of whom had been treated for kala azar some 11 years earlier.

In both a year or more after the cure was completed there began to develop the present condition consisting of patches of hyperpigmentation on the lower part of the abdomen, around the nipples and elsewhere and similarly extensive patches of depigmentation scattered about the body. In addition there occur on the body a small number of papules and some localized erythema, but nodule formation in the skin was absent. Leishmania were found in papules in one of the cases, both of which showed a definite eosinophilia, a frequent feature of cases of dermal leishmanoid. *C. M. W.*

STRUTHERS (E. B.), CHANG (H. H.), LIN (L. C.) & CH'EN (J. T.). **Antimony in the Treatment of Kala-Azar, and its Toxic Effects.**—*Chinese Med. Jl.* 1933. Nov.–Dec. Vol. 47. Nos. 11 & 12. pp. 1421–1432. With 1 plate. [17 refs.]

After a preliminary account of the use of antimony for therapeutic purposes and its application to the treatment of trypanosomiasis and kala azar, the authors pass on to consider their own experiences in the use of antimony in the last-named disease in N. China.

They have used a number of drugs, including sodium antimony tartrate, and the corresponding potassium, ammonium, aniline and lithium salts, sodium antimony thioglycollate, "212", antimosan, stibosan, aminostiburea, urea stibamine, stiburea, novostiburea, neostam and neostibosan. The reactions following the use of one or other of these drugs include fever, cough, vomiting, nausea, headache, lymphadenitis, diarrhoea, pain in abdomen, pain in legs, pneumonia, urticaria, gangrene of gums. The frequency with which these have occurred are shown in a table under the heading of the various drugs. Of these reactions the authors consider the most important as danger signals to be fever, enlarged and tender lymphatic glands, diarrhoea and necrosis of the gums. Of 700 cases treated 303 showed reactions, there being a total of 608 reactions in all. Of the 700 cases, 48 were treated with potassium antimony tartrate, 187 with sodium antimony tartrate, 39 with antimosan, 56 with stibosan, 93 with neostam and 228 with neostibosan. It was found that with a maximum adult single dose of sodium antimony tartrate of 0·08 gm. (antimony content 38·01 per cent.) there occurred almost double the number of reactions given by four times the dose of neostibosan (antimony content 42·0 per cent.).

Similarly with neostam, the average maximum adult dose of which was 0·2 gm., there were many more reactions than with neostibosan, the average maximum dose of which was 0·3 gm. *C. M. W.*

HU (C. H.). **Histopathology of Kala-Azar in Experimentally Infected Hamsters with Special Reference to Plasma Cells, Myeloid Tissue, Reticulo-Endothelial System, and Reticulum Fibers.**—*Chinese Med. Jl.* 1933. Nov.–Dec. Vol. 47. Nos. 11 & 12. pp. 1112–1124. With 26 figs. (2 coloured) on 13 plates. [15 refs.]

The authors have found that in addition to the well-known hypertrophy of the reticulo-endothelial system seen in hamsters as a result of kala azar infection, there is also an increase in the plasma cells in the lymphoid organs. They are found chiefly in the spleen pulp and in the medullary cords of the lymph nodes. They occur also in other organs, especially round the blood vessels. Though the reticulo-endothelial hyperplasia usually takes the form of infiltration by heavily parasitized cells, it may manifest itself as nodules, masses of cords of elongated or spindle cells free from parasites. Transition between the two types of hyperplasia can be seen. Another feature noted is the increase of myeloid elements in the spleen as a compensatory reaction to the crowding out of the bone marrow with reticulo-endothelial cells.

C. M. W.

CHUNG (Huei-lan) & CH'IN (K. Y.). **The Histopathology of Kala-Azar in Squirrels.**—*Chinese Med. Jl.* 1933. Nov.–Dec. Vol. 47. Nos. 11 & 12. pp. 1142–1145. With 6 figs. on 3 plates.

It has previously been shown by the authors that the squirrel (*Sciurotomias dividianus*) is susceptible to kala azar. It is now shown that the histopathological changes produced by the infection are similar to those found in hamsters and monkeys and are comparable with those in man. *C. M. W.*

DE (M. N.). **A Study on the Parasites of Kala-Azar and their Distribution in the Body.**—*Indian Jl. Med. Res.* 1934. Jan. Vol. 21. No. 3. pp. 627–634. With 9 figs. on 4 plates. [20 refs.]

A histological study of the organs of twenty-five cases of kala azar has shown that the leishmania are always parasitic in cells of the reticulo-endothelial system. These parasitized cells are constantly present in the spleen, liver and bone marrow, but only occasionally in other tissues which, when revealing these infected cells, have been the focus of some earlier inflammatory process. The author emphasizes his observation that parasites were never present in the endothelial cells lining the blood vessels. *C. M. W.*

NAPIER (L. Everard), SMITH (R. O. A.) & KRISHNAN (K. V.). **The Effect of a Plasmodial Infection in increasing Susceptibility to Leishmania Infection in Monkeys.**—*Indian Jl. Med. Res.* 1934. Jan. Vol. 21. No. 3. pp. 553–555.

With the object of testing the view that kala azar in man is secondary to some other infection, the authors have attempted to lower the natural resistance of *Macaca mulatta* (*Macacus rhesus*) and *Macaca irus* (*Macacus cynomolgus*) to *Leishmania donovani* by previous or subsequent inoculation with a malarial infection. The former monkey,

which possesses some natural resistance to *L. donovani*, was not rendered more susceptible by the plasmodial infection, kept in check by quinine treatment, while the latter, having a lower natural resistance to the kala azar parasite, appeared to be more susceptible as a result of the malaria. *C. M. W.*

NAPIER (L. Everard) & SHARMA (L. R.). **The Anaemia of the Leishmania-Infected Hamster.**—*Indian Med. Gaz.* 1933. Dec. Vol. 68. No. 12. p. 690.

In a previous paper (*ante*, p. 233) the authors described the results they had obtained in a cytological study of kala azar anaemia of man. Though a coloured plate of the reticulocytes of the blood of experimentally infected hamsters was given in the earlier paper, the results of the study of the hamster blood were not mentioned, as it was intended to make a more extensive series of observations in these animals. This, however, has not been possible, so in this note the authors point out that the limited results obtained show that on the whole the anaemia of kala azar in the hamster is similar to, though less marked than, the anaemia in man. Some figures of the cell counts in hamsters are given. *C. M. W.*

GIORDANO (A.). Le chat dans la transmission de la leishmaniose viscérale de la méditérranée. [**The Cat in the Transmission of Mediterranean K.A.**]—*Boll. Sezione Ital., Soc. Internaz. di Microbiologia.* Milan. 1933. Dec. Vol. 5. No. 12. pp. 330–332. [12 refs.]

The post-mortem examination for leishmania of 110 adult cats and 10 kittens in Catania, from parts of the town where human kala azar is most common and during the months of June and July when the cases in children are most frequently encountered, has failed to reveal a single infection. Particular care was taken to select only those animals which, from their poor condition and the presence of skin lesions, might have been suspected to be infected. *C. M. W.*

PREVITERA (A.). La leishmaniose viscérale canine à Catania. [**Canine K.A. in Catania.**]—*Boll. Sezione Ital., Soc. Internaz. di Microbiologia.* Milan. 1933. Dec. Vol. 5. No. 12. pp. 323–330.

PULVIRENTE in 1912 found that a percentage of 1·09 of dogs examined by him in Catania were suffering from kala azar. In the same year PANTO obtained a figure of 2·42 per cent. from 165 dogs, while the author now reports having found 6 cases of infection in 100 dogs examined. He comments on the differences between these figures and passes on to the general question of the much-discussed problem of the relationship between human and canine kala azar in the Mediterranean region. *C. M. W.*

MONACELLI (M.). Osservazioni e ricerche sul bottone d'Oriente in Italia centrale. [**Oriental Sore in Central Italy.**]—*Riforma Med.* 1934. Feb. 3. Vol. 50. No. 5. pp. 165–170. With 7 figs.

The author reviews the distribution of oriental sore in Italy as described in 137 records and finds that hitherto the disease has been limited almost entirely to the extreme south, in Sicily, Sardinia, Calabria,

Lucania and Apulia. A very few cases have been noted from areas further north as, for instance, Naples one case, Campobasso 2 cases, Ravenna one case. He now records the existence of an endemic area in the middle of the Adriatic coast with Teramo as its centre where he has seen over 160 cases. He discusses the clinical features of some of these cases and the differential diagnosis of the disease. *C. M. W.*

MONACELLI (M.). Il primo caso di leishmaniosi cutanea autoctona nella provincia di Forlì. [**First Case of Dermal Leishmaniasis in the Province of Forlì.**]—*Policlinico.* Sez. Prat. 1934. May 28. Vol. 41. No. 21. pp. 813–816. With 2 figs.

The discovery of the first autochthonous case of oriental sore in the province of Forlì in Italy is a further proof of the author's contention that the disease is endemic in the greater part of the Italian peninsula. The case is perhaps remarkable in that the patient was 75 years of age, the sore being a single one on the left cheek and having first made its appearance in December 1932. *C. M. W.*

MONTAÑES (P.) & NEGRO (E.). Dos casos de boton de oriente en la region Valenciana. [**Two Cases of Oriental Sore from Valencia.**] —*Medicina Países Cálidos.* Madrid. 1934. Feb. Vol. 7. No. No. 2. pp. 82–85. With 2 figs.

One of these cases was in a child 4 years of age and took the form of an ulcerating papilloma of the right cheek, while the other was in a woman 35 years of age, the lesion on the ulnar side of the hand having existed for 21 years. Cases of oriental sore have not hitherto been recorded from the district of Valencia. *C. M. W.*

BROWNFIELD (O. D.). **A Case of Oriental Sore.**—*Jl. Roy. Nav. Med. Serv.* 1934. Apr. Vol. 20. No. 2. p. 185.

The patient, a naval rating, was admitted to the Naval Hospital, Malta, with a four months' history of a sore at the inner end of the left eyebrow. Typical leishmania were found and healing followed intravenous injection of sodium antimony tartrate. Later in the same year the patient was re-admitted to hospital with a similar ulcer at the centre of the sternum. Both the Wassermann and Kahn tests were negative at the first entry to hospital but were strongly positive at the second. No source of infection could be traced and, if the disease was contracted in Malta, it would seem to be the first case of oriental sore from that island. *C. M. W.*

CHATTERJEE (Rabindranath). **Notes on the Treatment of Oriental Sore with Berberine Acid Sulphate.**—*Indian Med. Gaz.* 1934. Feb. Vol. 69. No. 2. p. 72.

The paper records the successful treatment with 2 per cent. solution of berberine acid sulphate (May & Baker's "Orisol") of some 2 dozen cases of oriental sore in Marwaris who had come to Calcutta from the Central Provinces. In a single sore 1 cc. of the solution is used by injection through 2 punctures. The process is repeated every other day till 12 treatments have been given. Not more than 2 sores are treated at any one sitting. For a patient with 2 sores it has been found that 12 infiltration sittings are necessary, involving a total of 48 punctures and a total dose of 24 cc. during 24 days. *C. M. W.*

LÖHE (H.). Beitrag zur Therapie der Hautleishmaniose. [**Treatment of Dermal Leishmaniasis.**]—*Med. Klin.* 1934. Feb. 2. Vol. 30. No. 5. pp. 158–160.

Two cases of oriental sore which proved refractory to treatment with salvarsan or antimony but which responded to injections of berberine sulphate. *C. M. W.*

DOSTROWSKY (A.). **The Diagnostic Value of Vaccine for Oriental Sores.** —*Harefuah.* 1933. Sept.–Oct. Vol. 7. No. 5. [In Hebrew pp. 205–211. With 1 fig. English summary p. 1].

Owing to the fact that in 23 per cent. of the cases of oriental sore in Palestine it is not possible to find leishmania because they are few in number or obscured by contamination, an attempt has been made to obtain a diagnosis by a skin test.

A vaccine containing one million flagellates per cc. (in 5 per cent. phenol) was injected intradermally in a dose of 0·1 cc. The result is regarded as positive if a papule not less than 0·5 cm. in diameter develops in 48 hours. A positive result was obtained in 97 per cent. of cases of oriental sore. A positive result was also obtained in 10 per cent. of cases free from oriental sore and in 5 out of 6 cases of leprosy.

Positive results are also obtained in persons who have recovered from oriental sore many years before. *C. M. W.*

MISCELLANEOUS.

YORKE (Warrington). Die Probleme der Arzneifestigkeit. [**The Problem of Drug Fastness.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Feb. Vol. 38. No. 2. pp. 55–66.

A valuable review is given of the work carried out in Liverpool during the past six years on the problems of drug fastness in order to determine (1) whether drugs act directly on parasites or produce some parasiticidal substance from the tissue of the host ; (2) whether when a strain of parasite becomes drug fast the primary change occurs in the parasite or in the host ; (3) the nature of the change. Pentavalent arsenic and antimony compounds are shown to be much less trypanocidal than trivalent compounds both *in vivo* and *in vitro*, those compounds which are highly trypanocidal *in vivo* acting also in high dilutions *in vitro*. The therapeutic activity of any particular arsenic or antimony compound is thus dependent on chemical constitution rather than on the action of the host's tissue. Germanin, however, though relatively inactive *in vitro*, is highly active *in vivo*. Strains of trypanosomes rendered resistant to a particular aromatic arsenic or antimony compound were found to be resistant also to other aromatic compounds of these metals but not to a number of non-aromatic compounds or to germanin. It is therefore concluded that the state of resistance is developed not against the metallic radical but against the aromatic nucleus. The nature of the change resulting in drug fastness is shown to be due to decreased powers of absorption on the part of those parasites which have become drug fast, this decreased power of absorption being in the nature of a mutation from the original non-resistant strain. The property of drug fastness remains constant even when trypanosomes have been passaged through the tsetse fly. *G. M. Findlay.*

CHOPRA (R. N.), GUPTA (J. C.) & CHOPRA (G. S.). **Pharmacological Action of Kurchicine (an Alkaloid of** *Holarrhena antidysenterica*).—*Indian Jl. Med. Res.* 1933. Oct. Vol. 21. No. 2. pp. 277–281.

The authors received from a firm of London chemists a white crystalline powder isolated from *H. antidysenteriae*, labelled *kurchine* hydrochloride. This they found to be very similar in properties to *kurchicine* described by GHOSH and BOSE. The crystals are very soluble in water and are therefore suitable for oral and parenteral administration.

To sum up the results of their study of this substance, kurchicine was found to be a general protoplasmic poison like emetine. Intravenous injections in animals produced a well marked fall in blood pressure. With toxic doses there was definite slowing of the heart with complete heart block. The vessels of the splanchnic area were dilated. Respiration was at first slightly stimulated, probably secondary to the fall in blood pressure but with large doses it quickly stopped, the heart continuing to beat. The plain muscle of intestine and uterus was stimulated even in high dilution. *A. G. B.*

PALTHE (van Wulfften). **Psychiatry and Neurology in the Tropics.**—*Malayan Med. Jl.* 1933. Sept. Vol. 8. No. 3. pp. 133–145. [Summary appears also in *Bulletin of Hygiene.*]

The psychic adaptability of Europeans in the tropics is very high. In the whole of the Netherlands Indian archipelago with its 250,000 Europeans there is no single sanatorium for " nervous patients " and there are only 652 Europeans who are inmates of lunatic asylums. Of these only a very small percentage have disturbances of which the origin may be traced with any probability directly or indirectly to the influence of the tropics.

In general, the psychoses of the natives do not differ much from those seen in Europe. Dementia paralytica develops even among the inhabitants of the remotest villages when they get infected with syphilis and there is no reason for supposing that the central nervous system of the native is unfavourable ground for the development of this disease. The schizophrenias of natives usually progress more quietly and smoothly than in European patients. True melancholics are seldom, if ever, seen among the natives but frequently among the Chinese. The author has never seen cyclic insanity. Infectious diseases and intoxications repeatedly lead to acute confusional insanity. The luetic psychoses in particular occupy a large and special place both in frequency and symptomatology. The difficulties of the European psychiatrist are great for besides the bar of language there remains a doubt whether there is not a specific oriental mental make-up which is different from that of the Western. After long years of work the European psychiatrist may get an insight into the inner thoughts and feelings of the group of people among whom he lives but certainly not into those of the folk, as a whole, of each tribe, with its own language or dialect, morals, customs and traditions, which inhabits Netherland India.

Amok is a method of reaction to toxic, infectious or emotional influences among natives, regardless of their race. In the author's opinion the character of amok is the standardized form of emotional explosion occurring in a person involved with his neighbours. In a modern hospital, where everything is carried on in European fashion and where an entirely different tone is maintained, amok has ceased. Latah is certainly not a psychosis and those who are afflicted maintain their social position and do their work perfectly well. The symptoms differ in degree but not in kind from the mimicking phenomena which we may observe daily around us and most of it is an artificial product, as was so much of the hysteria seen in Charcot's time. Koro is thought by the author to be an anxiety state in which the patient is in terror that his penis will shoot into his belly and that as a result he will die. After long hours of vigil, during which appropriate measures are taken, the attack gradually wears off but is repeated again and again. It is possible that the anxiety is not only as to death but also bears the character of a castration phobia.

Nothing is known of the actual number of insane persons in Netherland India but it is certain that the accommodation available is wholly inadequate. As a consequence observation hospitals and nursing homes are filled with the old and demented while new patients have to wait months before they can be admitted.

Among neurological patients there is a striking number of acute inflammatory affections of the central and peripheral systems. It is not improbable that a food factor may be found to play a large part in

many of the encephalopathies. Among all the millions of vaccinations performed not a single case of post-vaccinial encephalitis has been diagnosed. Acute poliomyelitis occurs only rarely and sporadically. Syphilis dominates the neurological picture and the number of patients suffering from one or other form of lues of the nervous system is, out of all proportion, high. Happily, reaction to treatment is favourable. One peculiar condition is a stroke in young men who are not suffering from lues, hypertension, arteriosclerosis, kidney or heart disease. Such seizures have a fleeting character. Persons attacked have low blood pressure and the cause may be sought in excessive smoking, overwork, living in warm places and exposure to direct sunlight. This condition with others associated with low blood pressure the author writes of as " essential hypotension " and holds to be of autonomic system origin.

E. D. Macnamara.

JORDAN (Edwin O.) & MCBROOM (Josephine). **Notes on Intestinal Flora in the Tropics.**—*Amer. Jl. Trop. Med.* 1934. Jan. Vol. 14. No. 1. pp. 27–32.

These notes call attention to the necessity for a systematic investigation of cases which are labelled " enteritis " and comparison of tropical cases with those of the temperate zone. " Enteritis and diarrhoea are common in Puerto Rico." This contrasts notably with a territory such as the Panama Canal Zone, where typhoid and dysentery have now practically disappeared, water is chlorinated, milk pasteurized, a good sewage disposal system exists and fly breeding is minimal. Various bacilli of the typho-dysentery group were isolated and examined in detail. The relations of these strains were determined and although in some cases the cultural relationships were definite they were not always serologically so definite. In the discussion of their findings the authors remark that probably " in tropical countries such as Puerto Rico . . . systematic bacterial examination would show a considerable number of unrecognized typhoid infections, and also many infections with various types of paratyphoid and dysentery bacilli. . . . In a well-sanitated tropical area, on the other hand, such as the Panama Canal Zone, . . . the bacterial flora of hospitalized adults does not differ noticeably from that of a similar population group in a northern city," such as Chicago.

W. F. Harvey.

RADSMA (W.), STREEF (G. M.) & KLERKS (J. V.). Over het zuurbase evenwicht bij tropenbewoners. Eerste mededeeling: Over de reactie der urine, in't bijzonder der onder " basale " voorwaarden verkregen morgenurine bij tropenbewoners. [**Acid-Base Equilibrium in the Tropics. Reaction of the Urine, especially Morning Urine, in the Tropics.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. June 7. Vol. 72. No. 12. pp. 798–807. With 5 figs.

——, —— & ——. Over het zuur-base evenwicht bij tropenbewoners. 2de mededeeling.—*Ibid.* 1933. Oct. 24. Vol. 73. No. 22. pp. 1357–1370.

An elaborate investigation and discussion of the reasons why the urine of native laboratory servants contrasts so strongly in its greater acidity with that of European residents (?) at Batavia.

The authors pay special attention to the morning urine and the 24 hours urine. They have considered such possibilities as the influence of

polyuria, of CO_2 loss, food differences, respiration, sweat secretion, etc. Native students and Chinese students occupied a position intermediate between the Europeans and the native servants, which seems to point to the conditions of living rather than race being the cause of the differences. The summary for the 24 hour investigation reads as follows :—

1. The hydrogen-ion concentration of the urine of native laboratory servants and the titrable acidity per kilogm. body weight and per unit of basal metabolism was greater than in European residents. 2. The excretion of ammonia per kgm. body weight and per unit of basal metabolism was greater, the excretion of fixed bases smaller, in native servants than in Europeans. 3. The phosphate excretion calculated on body weight was lower in native servants than in Europeans as also was the excretion of Cl and SO_4 per unit of basal metabolism. 4. These results indicate a deficiency of mineral constituents in the food and especially in fixed bases with a compensatory increased formation of ammonia in the body. 5. The excretion of organic acids in the urine in the native servants was higher per kgm. body weight than in Europeans but, reckoned per unit of basal metabolism, was the same as in Europeans.

W. F. Harvey.

REVIEWS AND NOTICES.

ANIGSTEIN (Ludwik) [M.D., Ph.D., etc.]. **Researches on Tropical Typhus. A Study of the Bacteriology, Serology and Epidemiology of the Disease.**—*Studies from the Institute for Medical Research, Federated Malay States, No. 22.* 1933. pp. vii+184. With 5 charts, 8 plates & 1 map.

Dr. Anigstein's work on the cultivation of the virus of typhus exanthematicus is well known. In this important and stimulating study he tells of the isolation of numerous strains of polymorphic organisms from men and rodents infected with tropical typhus, and he describes many experiments in support of his hypothesis that these strains, though they differ from one another in morphology, biological reactions and pathogenicity, all represent stages in the transformation of parasitic Rickettsia into saprophytic *Proteus X*.

He was specially seconded from the post of parasitologist at the State Institute of Hygiene in Warsaw for this investigation of the tropical typhus of Malaya, and from June 1929 until the end of 1930 he worked at the Institute for Medical Research in Kuala Lumpur. During that period 237 cases were notified ; 170 of these were of the rural, or scrub, type and agglutinated XK, while the remaining 67 belong to the urban, or shop, type and agglutinated X19. There were 19 deaths among the 170 rural cases, but only 1 among the 67 urban cases.

The virus of tropical typhus proved to be much less pathogenic for guineapigs than the virus of classical typhus ; only 10 per cent. reacted with fever, as compared with 92 per cent. in classical typhus, and the fever was shorter, lower, and more irregular. Loss of weight was more frequent, and was found in 25 per cent. A haemorrhagic gelatinous exudate about the polar fat of the testis and in the tunica vaginalis occurred in the majority of inoculated animals, but actual redness and swelling of the scrotum was observed in only 6 per cent. Numerous polymorphic gram-negative organisms were found in the exudate over the tunica vaginalis. These organisms were of two forms : (1) slender, spindle-shaped, polymorphic rods, and (2) minute, intracellular, bipolar-staining coccobacilli resembling small *Past. pestis*. The author found these organisms indistinguishable from the *Rickettsia orientalis* of tsutsugamushi demonstrated by NAGAYO, and he considers that they are " different phases of the Rickettsias—and represent the aetiological agent of the disease." Brain lesions, like those of classical typhus, were found in most of the guineapigs which had reacted clinically, but in cases where the scrotal reaction was most pronounced the brain lesions were least conspicuous.

In rats, a febrile reaction followed inoculation of the virus in about 20 per cent., but it was slight and lasted only 3 or 4 days ; on the other hand, 12 per cent. showed redness and swelling of the scrotum and Rickettsiae were found in the tunica vaginalis. A positive Weil-Felix reaction occurred in 28 per cent. of the rats inoculated with material from human cases of scrub typhus ; but, in many cases, it was X19 and not XK which was agglutinated, and here one calls to mind FELIX's warning (1933, *Trans. Roy. Soc. Trop. Med. & Hyg.*, Vol. 27, p. 166) that " the agglutination reactions obtained with *Proteus X* strains and the serum of wild or tame rats ought to be interpreted with utmost caution." A positive Weil-Felix reaction also resulted from the inoculation of infective material into rabbits, but the agglutination was

generally weaker and less regular than in rats. The author examined a number of rats caught in an area where tropical typhus of the rural or scrub form was present, with the result that he found testicular swelling and *Rickettsia* in 4·5 per cent. and a positive Weil-Felix reaction in 10·7 per cent. (though this was as often with X19 as with XK). In addition he cultivated organisms similar to XK from rats on 9 occasions. On these grounds he regards it as certain that the rat is the reservoir of infection.

The question of the vector remains unsettled; a mite, *Trombicula deliensis*, which B. A. R. GATER regards as a variety of *T. akamushi*, is suspected: but a volunteer, whom the author inoculated with an emulsion of 75 to 100 crushed mites collected in an endemic area remained healthy. Body-lice are not the vectors of tropical typhus; none were found on 472 hospital patients or on 6,459 school children examined in the Malay States. The author found, however, that they could be infected, though less readily than in classical typhus, either by allowing them to feed on patients, or by Weigl's method of rectal inoculation. During the second week of feeding, the lice swelled up and died, and extracellular Rickettsia-like organisms were found in the gut. He also succeeded in infecting lice with Rickettsia by feeding them upon a patient suffering from the tsutsugamushi disease.

Almost half the book is devoted to the organisms which Dr. Anigstein cultivated from patients, animals and lice during the course of his investigations. He is a firm supporter of the hypothesis enunciated by WEIL and FELIX, in 1921, that the virus of typhus represents the parasitic stage of *Proteus X*, and he states that the Proteus strains which he isolated from cases of tropical typhus were transformed into Rickettsiae when he inoculated them into lice. But he goes much further than WEIL and FELIX; for he has cultivated a large number of organisms differing from one another in their morphology, growth, fermentation reactions, and pathogenesis, which he regards as stages or steps in the transformation of typhus virus into *Proteus X*. He employed for the isolation of these organisms a medium known as Hottinger broth, which is a pancreatic meat-digest with the addition of ascitic fluid, and he used blood-ascitic-agar for the first subcultures. He succeeded in cultivating 76 strains in all. Thirty were from the blood, urine, or brains of human cases of tropical typhus, 2 were from lice, and 44 were from rodents. The cultures were gram-negative and highly pleomorphic, but they tended to fall into three groups; (1) fusiform rods with pointed ends; (2) diphtheroids; (3) minute coccal forms resembling Rickettsia. Among the 76 strains, there were 21 proteus-like swarming cultures; 18 of these were from passage animals and 3 were from patients' urine. The majority of the cultures had no serological relationship to *Proteus X*, but two strains—one isolated from a patient's urine, and the other from a rat inoculated with a patient's blood—appeared to be definite XK strains; they were agglutinated both by XK immune sera and by the blood of patients suffering from tropical typhus, and they also produced agglutinins for XK in rabbits.

Some of the other cultures, though they had no resemblance to *B. proteus*, and were not agglutinated by *Proteus X* sera, nevertheless produced a positive Weil-Felix reaction when they were inoculated into rabbits; but, as shown in tables 17 and 18, this was sometimes with XK, sometimes with X19, and sometimes with both. Moreover, the titre of agglutination was never above 1 in 250, while the serum of most of the rabbits agglutinated X strains up to 1/25 or even 1/125 before they were inoculated.

Dr. Anigstein found that the three different types of organisms produced different reactions in animals: (1) the fusiform rods had a low virulence, but gave a positive Weil-Felix reaction in rats; (2) the diphtheroids caused loss of weight, a testicular reaction, and perivascular nodes in the

brains of guineapigs; (3) the minute coccal, or Rickettsial, cultures produced high, sometimes fatal, fever when inoculated into guineapigs, and also a testicular reaction with minute coccal bodies resembling Rickettsia in the exudate. This type of culture was also very virulent for lice, and its inoculation into them resulted in "a most characteristic picture of classical Rickettsias." In support of his hypothesis that these strains occupy a position on the road of transformation from Rickettsia to *Proteus X*, Dr. Anigstein gives the history of two strains which were isolated in 1929. These strains formed isolated colonies on solid media, they fermented no sugars, and they had no serological relation to Proteus. They retained these properties for three years, but, in 1932, he transplanted them into broth from two-months' old agar cultures, and, 13 days later, he plated them out onto agar. He now found that they had been transformed into *Proteus XK*; they grew as spreading films, they fermented glucose with the production of gas, and they were agglutinated by an XK serum.

Dr. Anigstein's faith in the integrity of his passage animals is as great as his faith in the trustworthiness of his cultures. He believes that the viruses of the two forms of tropical typhus, the urban and the rural, are the same, and that "the diverse serological response of the infected organisms to XK and X19 may be interpreted as a result of antigenic transformation of the same virus derived from a common source, but carried probably by different hosts and vectors." In support of this hypothesis he describes the following experiment, in which he began by inoculating XK virus, and finished by finding X19. The blood of a patient who was suffering from an XK infection (rural) was inoculated into Hottinger's broth; 48 hours later this broth was inoculated into a guineapig; the brain of this guineapig was inoculated into a second guineapig; the brain of the second guineapig was inoculated into a rat; testicular washings from the rat were inoculated into a third guineapig; the brain of the third guineapig was inoculated into a human volunteer; this volunteer had a mild fever which lasted for ten days; his serum did not agglutinate XK which corresponded to the virus used at the beginning of this long series of transfers, but it agglutinated the O form of X19 at 1/125 and the H form up to 1/1,000. The author considers that this is cogent evidence of the transformation of XK into X19, but again Felix's warning as to the close association of rats with Proteus comes to mind. In connexion with the relation of X19 to XK, it is difficult to understand why Dr. Anigstein's XK immune serum agglutinated his standard OX19 culture more strongly than it agglutinated his standard OXK; and why his X19 serum agglutinated OXK more strongly than OX19, as shown in table XIII. They could not have been pure O strains.

Several other volunteers were inoculated with Dr. Anigstein's cultures, but the results do not appear very conclusive. For example, a volunteer was inoculated with a mixture of 4 cultures of the cocco-bacillary or Rickettsial type; namely 2 cultures from guineapigs inoculated with patient's blood, one from lice fed on a patient, and one from a "rat inoculated with head-lice passage virus." The volunteer had an irregular febrile attack which began 22 days later and lasted for 17 days. A positive Weil-Felix reaction of 1/25 for both XK and X19 appeared 9 days before the temperature began to rise; on the 10th day of the fever, the titres were only 1/50 and 1/125 and they rose no higher. In spite of these low titres, Dr. Anigstein concludes that the cultures representing "the Rickettsial type correspond in their pathogenic action to the original virus." The cultures of the Proteus type, such as those isolated from patient's urine, did not produce clinical signs which resembled typhus. A prophylactic vaccine was prepared from formolized cultures isolated from rats caught in an endemic area, and it was used with promising results to begin with, but the reviewer understands that it has since been withdrawn.

The book which is clearly printed, and illustrated with excellent half-tone blocks and microphotographs is the first of its kind to be produced locally in Kuala Lumpur. *William Fletcher.*

CALCUTTA. **Eleventh Conference of Medical Research Workers held at Calcutta from 27th November to 1st December, 1933.**—pp. ii + 332. 1934. Simla: Govt. of India Press.

Each year a Conference of Medical Research workers is held in India, the problems towards which attention has been directed are discussed, and future programs of research are considered. The eleventh conference was held in Calcutta in November 1933, and its proceedings are reported in the present volume. For ten years Major-General Sir J. D. GRAHAM has been Secretary of the Indian Medical Fund Association, arranging the conferences, and carrying out the multifarious duties connected with the activities of the Association. He now retires leaving behind him a record of fruitful and untiring service both in India and at Geneva.

The report which is now published covers a wide field. It is based upon reports by subcommittees on cholera, malaria, kala azar, plague, rabies and leprosy, and upon a number of notes by various authors relating to these and other enquiries.

That on cholera centres mainly on the enquiries on Bacteriophage, by Dr. ASHESHOV and Colonel MORISON. With regard to the latter the subcommittee were of opinion " that on the evidence at present available it is not possible for them to express an opinion on the value of phage in the prevention and treatment of cholera without a more detailed examination of all the facts in regard to the work which has been carried out on the subject during the last six years." They consequently recommended the appointment of an *ad hoc* committee, and the recommendation was adopted by the Conference.

The subcommittee on malaria dealt with the malaria surveys which were being carried out in the Punjab and in Sind, the primary object of those in the latter area being to obtain " a picture of conditions existing prior to the initiation of the Lloyd Barrage." Other enquiries on treatment, transmission, anopheline infectivity and on the influence of various epidemiological factors were discussed. These led to resolutions that, " apart from the heavy direct and indirect mortality caused by malaria, attacks of the disease are largely responsible for labour inefficiency," and that " treatment of the sick constitutes the first step in any antimalarial campaign, irrespective of any other methods employed."

With regard to kala azar, it was decided that, though research on this subject should be continued, the sum allotted for this purpose should be curtailed. Dr. R. O. A. SMITH, the Officer in charge of the enquiry, stated that " some investigators were prepared to accept the fact of the transmission by the sandfly in this manner [experimental transmission to the hamster] as proved, but the proof to others was perhaps not yet quite convincing."

There is nothing very novel in the report of the plague subcommittee. On the one hand enquiries of an epidemiological nature are being carried out in various directions, and on the other further investigations are being made of the biochemical characters of the vaccine, its standardization and its efficacy.

The rabies subcommittee devoted its attention mainly to a discussion of the policy of decentralization of treatment, and to the experiments which had been carried out at the Kasauli Institute, which have already been reviewed in some detail in this *Bulletin*. The subcommittee " viewed with satisfaction the progress made in decentralization of antirabic treatment, and advocated its extension

to those provinces where it has not yet been adopted." Experiments on the use of immune serum as an adjunct to vaccine treatment were adumbrated.

Amongst other subjects which were discussed were: sandfly fever, tuberculosis, goitre, oriental sore, maternal mortality and problems of general nutrition.

The report concludes with a summary of the evidence given by Major-General Sir J. D. GRAHAM to the League of Nations' Regional Health Conference at Cape Town (1932) on "India's point of view," with regard to the possible extension of yellow fever to that country, and a note by G. M. FINDLAY on immunization against that disease.

Much of the work brought before the Conference has already been published, and has been reviewed in the appropriate sections of this *Bulletin*. The remainder will no doubt appear in due course.

A. G. McKendrick.

WU LIEN-TEH & WU (C. Y.) [Edited by]. **Reports National Quarantine Service Series IV—1933.**—pp. iv + 264. With 28 figs. on 18 plates (1 coloured) & 7 charts. 1934. Shanghai, China: National Quarantine Service, 2 Peking Road.

This fourth annual report since the formal inauguration of the Service has, like its predecessors, the object of being a reliable guide to its manifold activities, of being "at the same time . . . a readable and not too technical account of that section of its work which is most closely connected with the commercial world" and of presenting original articles to scientific workers. A country which stretches, as we are told, "from latitude 53° North to 18° North, and therefore possesses every variety of climate from arctic conditions in Manchuria to tropical heat" in the southernmost province, must possess also a great variety of problems for the hygienist.

The original articles in this report deal mainly with cholera and plague, and the first of these is an erudite historical account of "Huo Luan" by the director, Dr. Wu Lien-Teh. This ancient Chinese term, if it were not purely applicable to cholera, certainly seems to have included that disease and seems to have been placed on record in the "Nei Ching" and to have been dated therefore B.C. 2697–2597. A very detailed analysis of Huo Luan is given. We may reflect that the syndrome of well-established cholera is a very striking one and that it might easily be recognizable as a disease even at that early period in the world's history. The introduction to the article begins, as do almost all treatises on cholera, with the statement: "It is generally believed that cholera . . . had its original home in the Valley of the Ganges." All countries from Russia in the West to China in the East seem agreed upon this. It might, however, be worth examining further into this statement, after admitting that the cholera vibrio was definitely discovered in Calcutta. We might even take the concluding sentence of this interesting article, with its recognition of cholera in China in remote antiquity, as suggesting the necessity of such a re-examination. "Hence our researches," says the author, "have confirmed in our opinion that Cholera, though rare was not altogether absent from ancient Cathay."

Many facts of importance are recorded in the article entitled, "Rat Flea Survey of Chinese Ports." These relate to the rodent and flea species found and also to their differential distribution in the ports of Shanghai, Amoy, Canton, Tongking and Hankow. "It would appear that *Ceratophyllus anisus* takes the place in China of the more common *Ceratophyllus fasciatus*" and again "*X. cheopis* appears to be able to adapt itself to a wide range of climate, but flourishes especially during the moist warm

summer." The author of this article, Dr. C. Y. Wu, is evidently convinced of the value of rat-proofing as an efficient anti-plague measure and his remarks on the subject are worth quoting: "Other factors," he says, "besides presence of infected *cheopis* are necessary for the spread of rat-plague (and later human plague) . . . For instance although there is no reason to suppose that the species and seasonal prevalence of fleas in Amoy and Canton have in any way altered during the past three decades . . . bubonic plague epizootics and epidemics have been extremely rare since the reconstruction of these areas along modern sanitary lines and the increasing use of rat-proof structures for goods storage and human habitation."

The remaining three original articles are worth studying. They have the titles, "Cholera and Related Vibrios in Shanghai Waters," "The Cholera Carrier Problem in Shanghai," and "Meteorological Factors in Cholera." A special article by Dr. J. W. Chun deals with "Recent Public Health Activities in Shanghai." It treats of various subjects, among them leprosy, and we may judge of the magnitude of this disease problem, as it confronts China, from the remark made by the author: "It has been said that of the three million lepers in the world, China has one million . . . and there are supposed to be about 2,000 lepers in Shanghai." The rest of the volume is taken up with matters which are mainly statistical or of local interest only. *W. F. Harvey.*

Printed under the authority of His Majesty's Stationery Office
by the South Essex Recorders, Ltd., High Road, Ilford.

(592) Wt. P3/124 1875 9/34 S.E.R. Ltd. Gp. 353.